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EDITORIAL NOTICES

CANCER AND TUBERCULOSIS: VI, THE RELATION OF THE WHITE BLOOD CORPUSCLES TO THE DEVELOPMENT OF MALIGNANT DISEASE.¹

By THOMAS CHERRY, M.D., M.S.,
Cancer Research Fellow, the University of Melbourne.

In my preceding paper⁽⁴⁾ dealing with the production of cancer in mice by the subcuticular inoculation of minute doses of tubercle bacilli, I used the polymorphic reaction caused by a spontaneous outbreak of pseudotuberculosis among the control animals for purposes of comparison with the lymphocytic reaction caused by the tubercle bacilli. It was shown that the tendency of the changes in the former case was to include in one syndrome the blood picture, enlarged glands and lymphoid bone marrow. On the other hand, the lymphocytic reaction following the inoculation of mice with

tubercle bacilli tended in the direction of lymphatic leucæmia, and was frequently associated also with neoplastic changes in various organs and regions of the body. During the past two years pseudotuberculosis has appeared, generally in chronic form, in more than half the cages of my stock of mice, affecting both the inoculated and control animals. The examination of microscopical sections of the gastro-splenic region of seven hundred mice indicates that this disease fulfils all the conditions necessary for a parallel experiment controlling the effects of the tubercle bacillus. While different classes of leucocytes are mobilized in the control and inoculated mice, they agree in the frequency with which the gastro-splenic region is affected and in the fact that in both instances the infection runs a chronic course. Both infections may make little difference to the average length of life, and produce no obvious indications of ill-health, so that the actual condition is discovered only after death. They are, therefore,

¹Read at a meeting of the Victorian Branch of the British Medical Association on October 29, 1930.
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examples of the chronic "carrier" condition of many laboratory animals referred to by Woglom:

It seems to be tacitly assumed that all laboratory animals are healthy. The truth is, however, that they suffer from serious infections of the digestive and respiratory tracts, and anyone who has had experience with them would probably agree in the presumption that any given mouse or rat is more apt to be infected than not.⁽⁵⁾

In this paper I compare the lesions in the gastro-splenic region of fifty mice, inoculated with tubercle bacilli and found to be free from pseudotuberculosis, with the same number of controls which had died of the latter disease. Type specimens have been chosen illustrating the apparent sequence of the lesions in each disease. The gastro-splenic region happens to be affected in both sets of mice, but for different reasons. The lymphocytic reaction of tuberculosis is most intense in the localities where the bacilli have been carried by the phagocytes. Hence the spleen is one of the principal depots, the areolar tissue along the splenic vein becomes infiltrated, the neighbouring omentum and mesentery exhibit the same changes, the lymph glands enlarge and adhesions between neighbouring organs may be formed; at the same time epithelial and other structures often show indications of proliferation.

In this outbreak of pseudotuberculosis the liver has been the principal focus of the disease. Direct extensions take place to the stomach and spleen, and hence there has been a corresponding reaction in the same set of tissues as are affected in the tuberculous mice—enlarged gastro-splenic lymph glands, adhesions involving the liver, stomach and spleen, and infiltration of the same areas of areolar tissue and fat. The mice inoculated with tubercle bacilli and those that have acquired the spontaneous infection may be directly compared. In addition, it is an advantage that the pancreas lies between the affected organs; its outlying lobules are regularly permeated by the advancing cells and invite a comparison of the changes in the epithelial cells associated with the two classes of leucocytes. The pancreas thus becomes an index of the changes that are in progress.

THE GASTRO-SPLENIC REGION.

In the mouse the pancreas is of the diffuse type common to most of the *Rodentia*. It approaches the ventral wall of the abdomen at the pylorus, but for the most part it lies across the spinal column, extending along the curvature of the stomach to the spleen. It may cover the root of the mesentery and part of both kidneys, especially the left. In this region small and large clusters of lobules extend like a fringe from these organs to which they are attached by delicate strands of connective tissue. The pancreas can hardly be described as consisting of lobes, as the clusters of alveoli vary greatly in size and arrangement. The secreting cells and structure of the alveoli are similar to the human type. The cells appear of cubical or low columnar shape in section, which usually shows six or eight cells in each alveolus. The nuclei are large and rounded, staining uniformly or showing half a dozen points of chromatin. Very fine clefts between adjoining alveoli give a characteristic appearance to sections

of the lobules, and these clefts are exaggerated in the preparation of the sections. Islets of Langerhans are common. The ducts belonging to each lobule are hard to find, and are never conspicuous in sections of the normal pancreas. Clusters of lobules are in apposition with the pylorus, especially on the hepatic side. From this point a well defined portion of the organ extends along the pyloric canal. Other clusters lie in the curvature of the duodenum. In the normal pancreas there is no infiltration with any type of wandering cell, and there are no lymph glands at least in young adult mice. Infiltration, enlarged lymph glands and ducts with conspicuous epithelium are common in pathological conditions.

MATERIAL AVAILABLE.

Fifty control mice (those that had not been inoculated with tubercle bacilli) have been found to be affected with pseudotuberculosis. These form the basis of one half of the series dealt with in this paper. For checking the appearances of the lesions in this group but not further referred to, there are 210 cases of pseudotuberculosis among the mice that have died after inoculation with tubercle bacilli.

The fifty mice forming the group inoculated with tubercle bacilli have been selected because they all present lesions in the gastro-splenic region. Most of these died before the first case of pseudotuberculosis had been found in any section of the experimental animals, so that the probability of the coexistence of the two infections is reduced to a minimum. As the mouse is very resistant to tuberculosis, the lesions produced never exhibit miliary tubercles or giant cells. Only three cases of tuberculoma have been found, and caseation is extremely rare. In fact, about one-third of the inoculated mice show no lesions after death that are recognizable to the naked eye, the inoculation apparently not affecting them in any way. Microscopical examination shows, however, that the small doses of tubercle bacilli are accompanied by a fairly constant infiltration of certain tissues with lymphocytes.

The doses used range about 100,000 bacilli. The method of inoculation and the management and previous history of the mice have been dealt with in my former paper.⁽⁴⁾ The site of inoculation is either the root of the neck between the scapulæ, or the inner aspect of the thigh.

"PSEUDOTUBERCULOSIS MURIUM."

Pseudotuberculosis murium was first described in 1894, the name being given to the nodules in the lungs which to the naked eye resemble miliary tubercles. Subsequent observations have indicated the existence of a group of organisms which vary somewhat in their staining reactions and pathogenic action. In my mice the bacillus agrees with Kutscher's original organism in being found in the muscle of the heart and in not being pathogenic for guinea-pigs, but it differs in forming lesions in and near the liver. It provokes a polymorphic reaction. The lesions are found in the lungs, pleura, myocardium, intercostal muscles and subcutaneous tissue; in the liver, peripancreatic fat and walls

of the stomach. In these lesions the percentage of polymorphonuclear cells ranges from 60 to 90.

The mice affected by this outbreak form a series complementary to those inoculated with tubercle bacilli, because they furnish a means of studying the effects of chronic suppuration in the internal organs by which a persistent infiltration with polymorphonuclear leucocytes is maintained. No method is known by which this condition can be produced by inoculation, for ordinary laboratory doses usually kill the mouse within a week, while very small doses do not seem to have any effect. About 10% of the fifty mice dealt with in this paper have healed or partly healed lesions in the liver, the necrotic area being replaced by fibroid tissue.

Pseudotuberculosis is an unfortunate name for this condition, as the organism has no connexion with Koch's bacillus. It has more definite affinities with some members of the paratyphoid group. Another organism, *Bacillus pseudotuberculosis rodentium*, affects guinea-pigs and rabbits, and is pathogenic for mice. It produces a polymorphic reaction, and some of its numerous varieties closely resemble *Bacillus pestis*.

THE CHANGES IN THE INOCULATED MICE.

The change associated with small doses of tubercle bacilli may be described under seven heads, three or more of which are present in each of the fifty mice, and they are so frequently associated and merge into one another so completely that they may well be successive phases of the one process. They are: (i) Infiltration of the areolar tissue; (ii) enlarged lymph glands; (iii) adhesions between the infiltration and adjacent organs; (iv) associated changes in the pancreas; (v) the pancreas may become malignant; (vi) active pancreatic cells may merge with adjacent structures; (vii) the lymph glands may become malignant.

(1) Infiltration of the Areolar Tissue.

Infiltration of the areolar tissue is very common in the inoculated mice, and acid-fast bacilli are found in the infiltration in four of the mice selected for the illustrations. Their presence supplies a plausible explanation of the assembling of the lymphocytes and suggests that their influence may be felt in lesions in the inoculated mice in which they cannot be demonstrated under the microscope. Figure I (Mouse 37) is taken from the tissue near the splenic vein, the adjoining spleen containing very large numbers of bacilli. Bacilli lie among the lymphocytes and red blood corpuscles in the venule which forms the central feature and among the masses of small round cells which infiltrate the fatty tissue. In one spot near the venule the clump is so large that it may be described as a colony.

(2) Enlarged Lymph Glands.

Enlarged lymph glands are very common in some part of the infiltrated area, being found in thirty-two of the fifty mice. When less than one millimetre in diameter they often have an uneven boundary on section, recalling the appearance of the empty spaces in the fatty tissue just described. When larger, they have a thin capsule, but seldom show

any signs of trabeculae. They sometimes contain large and small sinuses full of blood. They consist mainly of small cells of which the greater number are undoubtedly small lymphocytes, the nuclei of which give the characteristic dark colour to the sections. Lighter coloured areas contain cells with more cytoplasm, usually large lymphocytes, polymorphonuclear cells being comparatively scarce. The glands usually form a focus from which the infiltrating cells extend in all directions, and when these cells are traced from field to field they very often lead to one of the adhesions to be next described. Figure II is a general view of the infiltration in relation to the lobules of the pancreas.

(3) Adhesions to the Adjacent Organs.

Adhesions may form between the infiltrating cells surrounding the lymph glands and the stomach, liver or duodenum. The most common site is the pylorus and the adjoining parts of both stomach and duodenum. As a portion of the pancreas always lies in contact with the pylorus, this organ is almost invariably involved in the adhesion. A second adhesion or an extension of the first may be found at a little distance along the pyloric canal surrounding the enlarged gland already mentioned, or it may arise farther to the right along the duodenum. In these cases lines of infiltrating cells extend from the lymph glands in the pancreas to the adhesion or the whole area may be included in a continuous mass of cells. Adhesions to the liver are common, especially as part of that at the pylorus, and in several instances I have found one between the liver and duodenum. From these adhesions, lines of lymphocytes may be traced into the coats of the stomach, especially near the *sphincter pylori*. Elongate masses of these cells are found between the layers of the muscular coat, and they may then be traced in lines to the submucous tissue where collections become common. Infiltration of the walls of the stomach is found in more than half of the inoculated mice. The cells of the pancreas included in the adhesion and the epithelium of the stomach opposite to it are nearly always abnormal.

(4) The Associated Changes in the Pancreas.

The following summary of associated changes in the pancreas is a generalization from a study of the fifty mice. The average condition may be divided into presumably early and advanced cases, but from the detailed description of twelve examples it will be seen that the various lesions in a given mouse may be above or below the average both in number and intensity. Some of them may be emphasized and others nearly absent.

Speaking generally, the amount of the infiltration and the size of the lymph glands go hand in hand. The adhesions may be absent or restricted to one spot, or they may be the most noticeable feature in the sections. Sometimes the infiltration spreads almost uniformly between the alveoli; more frequently it affects zones enclosing masses of alveoli and lobules, so that this part of the pancreas appears more compact than usual. Changes are observed in both nuclei and cells. The former

become more vesicular than usual, and contain definite deeply staining points of chromatin. Or they may increase in size and stain deeply with hæmatoxylin and occasionally show indications of mitosis. The cells lose their normal shape and arrangement in the alveoli. They may become large with a single or with several nuclei, or they may subdivide, retain their prominent nuclei and become recognizable as pancreatic only by working back to normal lobules and alveoli. In a similar way the epithelium of the ducts becomes very prominent, exhibiting closely packed cubical cells with prominent vesicular nuclei, and they may appear at a distance from the clusters of alveoli. Finally, the infiltration and the adhesions may contain other cells beside the lymphocytes, many of them exhibiting various stages of organization and perhaps of early neoplasia. Many of these mice show changes which correspond to the remark of Ewing:

The parenchyma shows interesting changes. There may be a collateral or pre-existing hyperplasia of the pancreatic tissue which it is difficult to distinguish from invading carcinoma. (12)

Mouse 2 died thirteen months after inoculation, aged twenty months. Two large lymph glands consisting almost exclusively of lymphocytes are surrounded by lobules of the pancreas. Thick and fine lines of similar cells infiltrate the lobules, breaking up the normal architecture of the organ. There is a large, richly cellular adhesion to the pylorus from which lines of small round cells may be traced through the muscular coat of the stomach to join elongate masses of similar cells lying between the muscular fibres. From this point, other lines may be followed to a diffuse infiltration of the submucous coat. The changes in the pancreatic cells include a closing up of the alveoli into compact lobules, and many of the cells have large vesicular nuclei.

Mouse 10 died ten months after inoculation, aged sixteen months. This small wasted mouse had very large glands in the neck, extensive lesions in the thorax and a tumour in the gastro-splenic area 1.5 centimetres in diameter. The tumour consists mainly of small round cells with deeply staining nuclei, and a necrotic area contains immense numbers of acid-fast bacilli. In parts, it has a pseudocapsule formed of round and spindle cells and fine fibrille, outside of which bacilli are hard to find. By way of adhesions the round cells penetrate the capsule of the liver and the coats of the stomach and separate the pancreatic lobules. The sections of the lobules have lost their normal shape and those close to the capsule are quite unrecognizable, as the cells lie in irregular clusters or singly amidst the small cell infiltration. They are often elongated into oblongs or triangles with two or three large vesicular nuclei. Many of the large nuclei contain two or three small deeply staining points of chromatin.

Mouse 33 was inoculated with 100,000 bacilli and died four months later, aged eight months. There is a fibrocellular adhesion at the pylorus, containing many compact clumps of lymphocytes (Figure III). On the edge of the adhesion the lobules of the pancreas form compact masses with conspicuous nuclei (Figure IV). Within the adhesion they are often represented by a few alveoli or small clusters of cells still retaining active looking nuclei. Other fields of the gastro-splenic region show enlarged glands, intense lymphocytic infiltration of the areolar tissue and the walls of the stomach, adhesions to the stomach at the pylorus and along the pyloric canal, and widespread indications of proliferation of the alveoli and ducts.

Mouse 44 died thirteen months after inoculation, exhibiting a spindle and mixed cell sarcoma at the point of inoculation, similar growths in the subjacent axillary glands, and a very large liver half of which consists of sarcoma tissue of the same type. A large area of the pancreas lying between the liver and spleen shows the ordinary separation of the lobules from one another. Within the alveoli the cells have lost their normal arrangement and often also their normal shape. They are smaller and more irregular in outline and there is no trace of the two zones. The nuclei are large, very often vesicular, sometimes

exhibiting large nucleoli (Figure V). In other areas the tissues of the stroma also appear to be active, elongate nuclei and capillary blood vessels are distinct, while the prominent nuclei of the pancreatic ducts make these structures stand out in a manner quite unusual in the mouse. There is no great amount of small cell infiltration.

Mouse 849 died six months after inoculation, aged thirteen months. There is a large retroperitoneal tumour consisting chiefly of small lymphocytes mixed in some areas with much larger cells with very prominent nuclei. The liver is very heavily infiltrated with lymphocytes as are also the pancreas and walls of the stomach, with several large lymph glands of similar structure to that of the tumour. At the pylorus many lobes of the pancreas are adherent and continuous lines of lymphocytes may be traced into the muscular coat. The alveoli have closed their ranks and appear very similar to those shown in Figure IV. Other lobules are distended by an active lymph gland and exhibit another series of changes as described in subsection 6 *infra*.

Mouse 851 died nine months after inoculation, aged fifteen months. There are adhesions at the pylorus with a large lymph gland on the hepatic, and an area of the pancreas on the opposite side of the stomach. The pancreas surrounds part of the adhesion. The lobules have a very similar appearance to that shown in Figure V and many of the nuclei are large and vesicular. The infiltration is well marked in the areas close to the vessels, and here the sections of ducts with prominent and close-set nuclei are very conspicuous. The adhesion is more highly organized than usual, the arteries having thick walls, and all the vessels are relatively large. The blood count in one of these vessels is forty small lymphocytes and ten polymorphonuclear cells.

Mouse 9 died twelve and a half months after inoculation. The conditions in the pyloric region are very similar to the preceding case in regard to the firm well organized adhesion with large blood vessels. Many of these vessels are surrounded by lymphocytic infiltration which is sometimes collected into well defined masses of these cells. The muscular and submucous coats near the pylorus are infiltrated chiefly with small lymphocytes. Two medium sized lymph glands of irregular shape, consisting chiefly of lymphocytes, lie between the stomach and spleen. An area of the pancreas about six millimetres long and two millimetres broad extends along the pyloric canal. In it the alveoli and lobules have fused into larger areas, each representing from six to twelve lobules. Each of these presents a uniform crowded section very similar to the condition seen in Figure V. The nuclei are large and often vesicular, and many of the cells are much smaller than normal. Islets usually easily found in the pancreas are absent from the crowded areas.

Mouse 112 was a small mouse dying twelve months after inoculation with 25,000 tubercle bacilli. The chief lesion is an adenocarcinoma of the stomach, the walls of which are heavily infiltrated with small cells, and an adhesion is found involving part of the pancreas. The pancreas shows large areas of lobules with the clefts distinct, while the alveoli are replaced by cells lying close together, not arranged in tubules or circles, and with large nuclei which often almost fill the body of the cell. The vessels and ducts of the pancreas also have large and prominent nuclei.

Mouse 125 is another mouse with carcinoma of the stomach and a condition of the pancreas very similar to that just described. The parts showing most evidence of change lie between the liver and a large lymph gland. Here the pancreatic cells with prominent nuclei are often confluent or have remained single and assumed triangular, elongate and other bizarre outlines.

(5) The Pancreas May Become Malignant.

Six examples of malignant change in the pancreas are included in the fifty mice, and as I can find only one case of carcinoma of this organ hitherto reported (6) the presumption is that, provided my diagnosis is correct, some special cause is operating on these mice. From what has been said about the stages exhibited in the gastro-splenic region, it appears that either the secreting cells, the epithelium of the ducts, or the stroma may take the lead, so that carcinoma simplex, duct carcinoma or scirrhus may

result. The distribution of the lobules which are malignant or greatly changed from normal conveys the impression that the agent causing the change is not equally distributed, but is acting with varying degrees of intensity upon different parts of the organ. The accompanying line block shows the actual size of the areas which have become malignant, in regard to which it may be pointed out that on the basis of comparative weight five millimetres in a mouse is equal to at least three inches in a man.



Mouse 83 died three and a half months, and Mouse 894 eleven months after inoculation. These are two cases of *carcinoma simplex* (Figure VI). The extreme changes are found in areas about five millimetres in diameter in which all signs of normal structure except the islets are completely lost. The pancreatic cells are changed into a uniform sheet of medium sized epithelial cells with large and deeply stained nuclei which occasionally show signs of subdividing. Many of the cells where they are closely packed together are oval, elongate, tailed or spindle shaped, and others are polygonal. Beyond the main area there are signs of a similar change in adjoining lobules; many of these resemble Figure V. The widespread occurrence of these changes is very marked in 894, in which mouse the infiltration is most marked. There are two small lymph glands in 83, and three in 894, which also shows much infiltration of the coats of the stomach.

Scirrhus Carcinoma (Mouse 563, inoculated in inner aspect of thigh, died eight months after inoculation, aged sixteen months). The naked eye lesion was a bean-shaped mass one centimetre long, in the mesentery. On section, this has a firm fibrous appearance, dotted with small pink and dark red dots. Microscopically the mass is adherent to the large intestine and to the pancreas, and exhibits a moderately cellular fibroid stroma in which there are many large and small densely crowded cellular areas. Some of these lying near the wall of the intestine are packed with cells of the small lymphocyte type, and from the large collections lines of similar cells extend into the fibrous tissue and to the bases of the intestinal glands. The elongate or irregularly shaped areas of epithelial cells may be traced along the edge of the stroma to comparatively normal acini of the pancreas. In the section the cells are densely crowded, and do not closely resemble those of the parent organ. Some areas have a tendency to a tubular arrangement. The nuclei are large in proportion to the cells and have every appearance of vigorous activity. In Figure VII the outlines are taken from a photograph and the details filled in by hand, the nuclei being too crowded to photograph satisfactorily.

Three other cases have been already described and illustrated.⁽⁴⁾ They include a large mixed tumour with many areas of duct carcinoma and secondaries of the same character in a gastric lymph gland and two cases of *carcinoma simplex*.

(6) Active Pancreatic Cells May Merge with Adjoining Tumours.

When the pancreatic alveoli are near an actively growing neoplasm such as a malignant gland surrounded by lobules of the pancreas, the growth of the gland forces the lobules to spread out on its surface until in section many parts appear to be covered by an imperfect capsule of stretched-out pancreatic alveoli. As the process advances, the alveoli become surrounded by the actively growing lymphoid cells, but the pancreatic cells and nuclei still remain easily recognizable. The nuclei are

sometimes large and vesicular, sometimes equally large, but stain deeply and uniformly. Ultimately the large deeply stained nuclei with very small traces of cytoplasm blend with and become lost in the general cells of the tumour. The explanation of this condition found in eight of these mice is not clear, for the pancreatic cells do not form a tumour on their own account, but appear to join forces with the tumour in apposition with them. Such phenomena have long been noticed in connexion with malignant tumours in man. In the old days a good deal was heard of the "spermatic" influence of tumour cells by which they compelled some of the cells in contact with them to become similar to themselves. In quite modern days, C. C. and J. M. Twort in their report on tumours produced by local irritation in 29,100 mice, remark:

We have come to the conclusion that the change in the morphology of the cells is often due to the influence of neighbouring cells—a fundamental biological phenomenon.⁽⁷⁾

(7) The Lymph Glands Themselves May Become Malignant.

Lymphocytoma, lymphosarcoma and mixed cell sarcoma form a group of tumours which include the most common neoplasms found in this region of these mice, whether inoculated or control. The evidences of malignancy vary greatly and merge completely from a simple enlarged gland to the largest and most widely distributed tumour found in these mice. In size it may fill the greater part of the abdomen; it may invade the liver, stomach and kidney as well as the pancreas, and the same type of growth may affect most of the lymph glands in the abdomen. Secondaries may be formed in the lungs, mediastinum, pleura and intercostal muscles, as well as in the lymph glands in the neck, axillae and inguinal folds. It is the actively growing tumour of the lymph gland type which expands and ultimately incorporates the pancreas in its tissues in the manner just described.

These lymphoid tumours are usually associated with an intense infiltration of the pancreatic region which is almost exclusively lymphocytic in character. As this paper does not deal with tumours except those of the pancreas, I propose to leave this aspect of malignant changes in mice for further discussion, especially as the subject is closely related to leucæmia and its allies.

THE PSEUDOTUBERCULOSIS GROUP.

As already mentioned, this material has been made available by the fact that in this outbreak the little nodules occur not only in the substance of the liver, but also upon its gastric surface. The involvement of the pancreas follows simply from its proximity. On the average the infiltration and adhesions are very similar in size to those of the inoculated mice, but occasionally the gastro-splenic region is filled with a mass which half buries the spleen and stomach and completely conceals the pancreas. This mass appears to have been formed by the aggregation of great numbers of the nodules. It has a fibroid capsule rather poorly organized with many little areas of granular structureless material, apparently the centres of the original nodules. The enlarged

lymph glands are less conspicuous in these mice than in the former series, and when stained the uniform dark colour due to the crowded nuclei of lymphocytes occurs at most only in patches.

Mouse 213. There is a large tumour formed by dozens of pseudotuberculosis nodules encircling the pylorus and involving the adjoining part of the stomach and liver. The pancreas is in all parts infiltrated with polymorphonuclear cells and red blood corpuscles, in places the lobules are literally lying in a pool of blood, so that it seems probable that oozing from a vessel had been going on for some time before death. The lobules are everywhere separated from one another, and when embedded in the infiltration a low power view of the situation is presented in Figure VIII. This lies between the wall of the intestine and an area of blood. The nuclei of the collections of lobules are for the most part deeply stained, but there are others in which the fainter nuclei form circles and oblongs. Two large bile ducts with prominent nuclei lie between the lobules. The deeply stained nuclei nearly always occupy the outer zone of the cells, sometimes they are vesicular. Many of the cells are partly detached from their regular position in the alveolus and cling to each other in small irregular groups. Where two or three detached cells lie in the infiltration, the nuclei are often almost bare of cytoplasm. The nuclei of the bile ducts stain rather faintly, the chromatin being collected into a circle. The greater part of the infiltration affords a good study of organization, plasma cells, fibroblasts, fibrillae and capillaries being abundant. At the pylorus, the muscular coat of the stomach is much infiltrated with polymorphonuclear cells, and close to it there are two small lymph glands in which also the polymorphonuclear is the predominant cell.

Mouse 305. This is another large tumour filling the greater part of the gastro-splenic area and causing the disappearance of large areas of the pancreas. The remains of that organ can be identified in the infiltration between the tumour and lobes of the liver, and between the tumour and the stomach. The lobules can be traced as elongate collections of alveoli, and in parts the alveoli are reduced to elongate collections of cells, often with confluent cytoplasm or with faint indication of their division into separate cells. In one field of the high power showing the edge of the tumour and of the liver there are the remains of fifteen pancreatic alveoli. In about half of them, the cytoplasm has fused completely forming a uniform cell body. The nuclei are fairly uniform in size, rather smaller than those of the normal cell, but much larger than those of any of the leucocytes. Where five or six of them occur together, they generally form a horseshoe or a rosette.

Mouse 286. An adhesion at the pylorus in which a number of the lobules of the pancreas are embedded lies in a sharp kink between the stomach and duodenum. It is well organized with many thick-walled arteries and wider veins, and is firmly attached to the muscular coat at the sphincter by strands of fibrocellular tissue. Masses of leucocytes, chiefly polymorphs, are found in the muscle, and long lines of similar cells can be traced from them between the muscular fibres. The fibrillar tissue is richly cellular with round elongate and rod-shaped nuclei (Figure IX). The lobules of the pancreas, which are most deeply embedded in the adhesion, have retained their normal shape to a greater extent than those just described; but in parts the extension of the fibroid tissue between them is associated with the arrangement of the lobules in lines, or it has completely isolated some of the alveoli from their lobule. These alveoli are often reduced in size, showing three or four misshapen cells lying together, with large deeply staining nuclei, but no arrangement into outer and peripheral zones. Alveoli answering to this description are found lying by themselves deep in the adhesion, and in these the nuclei have become smaller, more numerous, and sometimes difficult to identify as pancreas, a condition to be described more fully in the next mouse.

Mouse 299. In this mouse all the stages involved in the disappearance of the pancreatic cells and alveoli may be followed in an adhesion at the pylorus. Towards the peritoneal surface of the adhesion the infiltration consists mainly of polymorphonuclear cells, and in some fields (Figure X) plasma cells and fibroblasts are also common, and traces of developing fibrillae and blood vessels are seen, the lymphocytes constituting about 15% of the cell count in this area. In the vicinity the pancreatic alveoli are little altered, but they are infiltrated with polymorphonuclear cells and dense isolated clusters of these cells

may also be found. The alveoli become less normal as the muscular coat of the stomach is approached, where they become widely separated and cannot be recognized as parts of the pancreas. Under the low power, the deeply stained nuclei form circles, ovals and what look like irregularly convoluted tubules lying in a cellular fibrillar tissue. At this magnification, the appearance suggests the irregular lobules of an epithelial neoplasm. The high power shows the nuclei to be so densely packed together that it is difficult to photograph them (Figure XI). They are resolved into irregular collections of nuclei apparently in various stages of pyknosis. Many form more or less complete rings; others solid mulberry masses. Single deeply stained nuclei are common, and several lying close together appear as an irregular blot by the diffuse action of the hematoxylin. Little or no cytoplasm is seen either about the masses or attached to the single nucleus. The bizarre shapes of the bunches of nuclei suggest retrogression rather than development, especially as these fields contain many indications of active organization, for the pancreatic alveoli are progressively affected—least so at the peritoneal surface of the adhesion and most at the surface of the stomach.

Mouse 326. A small pseudotuberculosis nodule in the liver and a well organized adhesion between the pylorus and pancreas are seen in this section. The adhesion consists of fibroid tissue in which are many blood vessels. The lobules of the pancreas lying in it are easily recognized, but the alveoli are more widely separated than usual. On the edge of the adhesion some of the pancreatic cells lying among the fibrillae consist of a normal nucleus lying in a pear-shaped cell. There are no indications of activity in the nucleus. An adjacent lymph gland is not densely crowded with nuclei and contains many polymorphonuclear cells. In the duodenum Brunner's glands are far more cystic than normal: their nuclei are unchanged.

Mouse 332. There are many nodules in the liver and walls of the stomach with widespread infiltration and adhesions. Pancreatic cells are embedded in the inflammatory tissue on both aspects of the stomach. The lobules are becoming indistinct, and the alveoli broken up until all signs of their identity disappear. On the edge of the adhesions the polymorphonuclear cells represent 80% of the infiltrating cells.

Mouse 385. A large cluster of nodules lies between the organs in the gastro-splenic region. A portion of the pancreas adjoining the stomach is infiltrated and is disappearing among the polymorphonuclear cells and fibroblasts. In all parts of the infiltration the polymorphonuclear cells greatly preponderate.

The foregoing mouse illustrates what may be called the death of the pancreatic cells on active service occurring apparently comparatively soon after inclusion in an adhesion. These cells disappear also by pressure in well organized adhesions when the cells and nuclei retain their typical appearances almost to the last. This stage is illustrated in Figure XII (Mouse 379). Here the cells, even when isolated, can be easily recognized as pancreatic sometimes a little altered, sometimes nearly normal. The appearance of the alveoli is also not far from normal. But these isolated alveoli are closely surrounded not only by crowds of small cells among which there are many fibroblasts, but by strands of the organizing fibrillae many of which are in actual contact with the cells.

DISCUSSION.

These observations enable us to compare the action of two chronic irritants in the mouse, the one producing a lymphocytic and the other a polymorphic reaction. In both instances the same region is affected, the numbers of white blood corpuscles found in the tissues appear to be comparable, and the changes in the secreting cells and ducts of the pancreas or the formation of adhesions may be followed in both sets of mice. The spontaneous appearance of the infection, which mobilized the polymorphonuclear cells in in-effect

a parallel experiment controlling the results observed to follow the intentional mobilization of the lymphocytes by inoculating the mice with tubercle bacilli. It is advisable to give a brief account of the facts relating to each class of leucocyte in the mouse and in human beings before treating of the significance of the results which have just been described.

In man the total numbers and relative proportions of these cells are known, and any considerable departure from normal raises the suspicion of some disturbance of health. In the mouse the lymphocytes are nearly always at least twice as numerous as the polymorphonuclear cells, but no precise statement can be made as to what is the normal count. A prolonged series of examinations of the blood of the mice used in these experiments was recently made by Dr. Marion Wanliss, who found that two counts taken from the tail of the same animal at intervals of two hours often presented totally different pictures. The average was ten million red and eleven thousand white cells per cubic millimetre, but this average was arrived at from a set of singularly discordant individual counts. Hence it is not safe to assume that the blood picture found in section after death is similar to that exhibited by the mouse, say, a few days before death. This anomalous result is similar to those obtained in other laboratories. For instance, at the Crocker Institute, an "enormous" number of counts led to the conclusion that a normal standard for mice could not be established, as no two mice had even approximately the same blood picture.⁽⁸⁾ The failure to establish a blood standard is only partly accounted for by the small size of the animal and the difficulty of reducing the margin of error in the technique to a corresponding extent, as an average "drop" of blood from the mouse is equivalent to about 100 cubic centimetres from a man. In addition, I am inclined to think that certain tissues in this animal, which is the smallest of the mammals, are not standardized as rigidly as in the larger members of this class. The more I know of the bone marrow, lymph glands and spleen, the less I am prepared to define any standard as being the normal. In healthy mice the pancreas and adjoining areolar and fatty tissue are free from infiltration with cells of any kind. In sections in which collections of cells appear I have taken an arbitrary standard, 75% as marking an increase in the lymphocytes, and one of 40% as indicating an increase in the polymorphonuclear cells.

The Lymphocytes.

The lymphocytes usually appear in mammalian tissues in response to a chronic irritation of mild intensity. In 1902, Maximow in his work on inflammation hit upon an experiment which is typical of their general behaviour. By the introduction of aseptic foreign bodies he showed that an early active emigration from the blood vessels took place. Some of these lymphocytes which crowded round the body developed large mononucleated cells among which the fibroblasts appeared at a later stage. In 1912, Da Fano;⁽⁹⁾

working in London on transplanted cancers in mice, found that:

The lymphocytes are not attracted by healthy foreign cells or by necrotic tissue, but rather by a tissue in a special stage of the process of necrobiosis. The polymorphonuclear cells under aseptic conditions exercise no phagocytic action, but degenerate rapidly *in situ*.

Some of the most typical examples of intense lymphocytic infiltration in my inoculated mice are adjacent to parts in which a few acid-fast bacilli may be found after a prolonged search. Gye and Kettle⁽¹⁰⁾ observed that much larger doses than those which I use provoke a polymorphic reaction at first, followed by the appearance of the lymphocytes. In mice after subcutaneous injection of a "fine emulsion" large cells (mostly polymorphonuclear cells with a few mononuclear cells) appear at the point of inoculation. These are actively phagocytic and most of them are seen to contain bacilli. With still larger doses (dense emulsion) intense crowding of polymorphonuclear cells occurs in from nine to twenty-four hours. These cram themselves with the bacilli and are surrounded by a dense zone of large and small lymphocytes. The central area consists of the *débris* of disintegrated cells and bacilli amongst which mononuclear cells and fibroblasts appear, and a wall is gradually organized, but the whole process causes very little tissue reaction.

In man, a decided increase in the number of lymphocytes in the blood is found in acute lymphatic leucæmia, and a smaller increase in some acute diseases as small pox, typhoid fever and whooping cough, and in certain phases of tuberculosis. In the tissues local collections appear in subacute and chronic conditions, such as fibrous adhesions and around acute inflammatory foci which have become quiescent. They are found around syphilitic vessels and about miliary tubercles and lupus ulcers. Mild forms of injury cause them to appear in the deeper layers of the skin as is seen in tar-painting, X ray dermatitis and slight injury by heat.

The Polymorphonuclear Leucocytes.

The polymorphonuclear leucocytes are the main line of defence of the mammalia against bacteria. They are mobilized by wounds as soon as these have become infected with pyogenic cocci and by many infective diseases of which two are of interest in connexion with the mouse, plague and various forms of pneumonia. In the mouse, these cells appear to have attained a high standard of efficiency. The pus cocci in the neighbourhood of a wound or skin abrasion are gathered up by the polymorphonuclear cells in such numbers that the cell is crowded with them and the nucleus completely obscured. Some of my mice exhibited the picture of a chronic pyæmia, as many of the little necrotic areas had softened into pus. Bronchopneumonia is one of the commonest causes of death in these mice; at the time of death large areas of the lungs are solidified, recalling the naked eye appearances of croupous pneumonia. This condition is often found associated with the nodules of pseudotuberculosis.

The polymorphonuclear cells are the most stable of the cellular constituents of the blood. In rats

and mice absence of water-soluble vitamin B from the diet leads to atrophy of the lymphoid tissue throughout the body and to a marked fall in the number of lymphocytes in the circulating blood. The polymorphonuclear cells are not affected. This change leads to a condition of marasmus.⁽¹¹⁾ The rule that the infiltrating polymorphonuclear cells do not develop into any other form of tissue cells seems to hold throughout the mammalia. Philosophers have surmised that the mobile shape of the nucleus is an adaptation to allow of the easy passage of these cells through the walls of the blood vessels and thus facilitate their rapid appearance at the site of injury.

The Lymphocyte and Malignant Disease.

Observations on malignant disease may be divided into four different phases, the tumour being: (i) spontaneous, (ii) caused by irritation, (iii) transplanted, or (iv) transplanted into an immune animal.

1. In spontaneous tumours, Ewing regards the infiltration as a low grade inflammatory reaction, "a highly significant feature of malignant tumour growth which must be regarded as a defensive process . . . yet about many epitheliomas that are making little progress one finds a thick barrier of lymphocytes, and in carcinoma of the breast islands of tumour cells enclosed in masses of lymphocytes and presenting clear signs of degeneration are common. . . ." Uncomplicated tumours provoke no uniform local reaction, and accordingly they seem to have no power of attracting leucocytes into the general circulation. The later stages—ulceration, degeneration and necrosis—bring on a leucocytosis which is usually polymorphonuclear.⁽¹²⁾

In recent accounts of the early stages of papilloma and carcinoma of the stomach and large intestine, attention is drawn to the frequency of lymphoid infiltration of the muscular and submucous coats with collections of similar cells at the base of the tumour. Such collections appear to produce the initial bulging forward of the *muscularis mucosae*. Such observations as "small round lymphocytes in abundance" and "a very high proportion of leucocytes in the blood" are frequently found. I drew attention, in an earlier paper, to these findings, and claimed that they are very similar to those found in my inoculated mice.⁽⁴⁾

In man, lymphocytes are prominent around an area of lupus, in X ray dermatitis and in burns which are not sufficiently severe to raise the epidermis.

2. In the production of skin cancer in mice and rabbits by means of tar the details of the reaction differ in these two animals. Attention has been given almost exclusively to the changes in the epithelial cells, the connective tissue, and the reticulo-endothelial system. Local inflammatory centres in the subcutaneous tissue are noticed, and lymphocytes become conspicuous as the condition becomes chronic. Polymorphic leucocytes, later replaced by lymphocytes, wander into the tissue of the corium and subcutaneous fat within two

days of the first application, and the fibrous bundles increase, so that the corium becomes fibrous and rich in cells.

3 and 4. The lymphocytes in relation to transplanted tumours in susceptible and immune animals may be taken together. In 1908, Wade drew attention to their appearance in an alveolar sarcoma of the dog, with which he was carrying out transplantation experiments.

The presence of lymphocytes and their derivatives throughout the tumour, and forming extra vascular accumulations beyond its border occurs also in true malignant neoplasms, and is another point of resemblance in the histology of these tumours with similar sarcomata found in human beings.

Grafts deposited in the tissues of dogs that had recovered from a former transplant were flooded almost at once by cells of the lymphocyte group, the nodule being "borne away on a lymphocyte tide". He suggests that the recession and immunity were the result of cytolysis of the tumour cells, this being brought about in all probability by lymphocytes and their derivatives.⁽¹³⁾

Da Fano's observation that the lymphocytes gathered about tissue which was aseptic and half dead has already been noticed. When such material was capable of eliciting immunity to a cancer graft, the lymphocyte response was greater than it was in respect of tissue of similar kind which had not become possessed of the property of imparting immunity. But a second inoculation of the tissue which had imparted immunity to the mouse did not provoke a second lymphocyte response.⁽¹⁴⁾

Upon this foundation, many years of work have been devoted to the lymphocytes. Their reaction to spontaneous tumours and to irritation cancers might have been passed by as merely a phase of the inflammatory reaction towards a condition too mild to provoke the polymorphonuclear cells. But the fact that they cannot be induced to attack a second implant seems to indicate that they stand in some special relationship to the malignant process and that they lose interest in it with the development of immunity. Murphy and his colleagues found that there were several methods by which the lymphocyte count of the mouse could be increased or diminished. With a low count these animals were made more susceptible than usual to cancer grafts and tubercle bacilli. Conversely, with a high lymphocyte count they became more resistant to both these agents. Moreover, when a localized lymphocytic reaction had been brought about by X rays and other means, the local reaction protected the animal against grafts placed in that area. Conversely, artificial inhibition of the local reaction allowed the implanted graft to grow. Hence the lymphocyte appeared to be the chief agent for the defence of the animal.⁽¹⁵⁾ An imposing array of first-rate names can be cited in support of Murphy's position, at all events to the extent of making the lymphocyte one of the essential factors in defence. On the other hand, many regard these cells as being casual visitors attracted by the graft as they would be by any other aseptic foreign body. The infiltration with small round cells occurs in both advancing and receding tumours, and on Murphy's theory it is

difficult to explain the frequency of metastases in the lymph glands where the lymphocytes are supposed to be arranged in dense masses in the very spot where they are formed. Facts observed in the rat, rabbit and guinea-pig are held to discount some of the experimental results obtained from the mouse. Woglom, who has been working half his lifetime at the cancer problem, sums up in his recent critical review:

It does not seem to me that Murphy has succeeded entirely in establishing his position, in spite of the ingenuity with which his experiments have been planned and the patience with which they have been carried out. Yet, on the other hand, I do not think that any of his critics have entirely dislodged him. After all there is something to be said for the lymphocyte.⁽¹⁶⁾

Growth Stimulating Substances.

These substances have been steadily investigated during the present century and have proved perhaps the most fruitful application of the technique developed in connexion with cell cultures. In 1902 it was discovered that yeast cells, if thoroughly washed, refuse to grow in a suitable sugar solution, but promptly responded to the addition of a trace of yeast juice. Within the next few years Cropper and Drew⁽¹⁷⁾ showed that the amoeba and other protozoa could be stimulated to energetic growth and subdivision or induced to assume the resting stage. Large numbers of pure chemicals and mixtures of substances were found to have a stimulating or inhibiting action, and working hypotheses regarding their share in the causation of cancer and other tumours were gradually elaborated.⁽¹⁾ In 1910, Carrel and Burrows⁽¹⁸⁾ found that the addition of embryo extract to a culture of the cells of the adult animal increased the rate of growth up to forty-fold, and nearly as great acceleration resulted from the juice of organs containing much lymphoid tissue and extract of the lymphocytes obtained from cases of tuberculous pleurisy. In 1922, Drew showed that the stimulus was enhanced by careful incubation of the piece of tissue, and accounted for the change by the autolysis of some of the cells which was brought about by this treatment.⁽¹⁹⁾

Carrel's review of the mechanism of the formation and growth of malignant tissues⁽²⁰⁾ begins with the observation that two factors require to cooperate to bring about a cancer—local irritation and a special condition of the tissues (including cells supporting tissue and fluids). He set about separating these factors by working with pure cultures of various types of cells, with Rous sarcoma, and a number of carcinogenic substances. A fragment of Rous sarcoma produces a mixed growth of polymorphonuclear cells, macrophages and fibroblasts. Pure cultures of each of these were obtained, and it was found that the macrophage was the cell which produced the tumour in chickens. Similarly the cells of a subcutaneous tar sarcoma in the rat gave a growth of macrophages which were apparently identical with those of Rous sarcoma, but a tumour could not be produced in rats by these cells alone or in combination with the other cells isolated from the tumour. The culture of the macrophages from Rous sarcoma differed from that

derived from the tar sarcoma. Attempts to transform fibroblasts and macrophages into sarcoma cells by adding a trace of tar to the cultures were uniformly unsuccessful.

In the case of carcinogenic substances, "it is plausible to think that products of the bacteria, parasitic worm, or something from X ray burns may be the factor which determines the onset of malignancy." Repeating the old experiment of adding a localizing agent to his cultures, he inserted a shred of woollen cloth soaked in very dilute Rous filtrate beneath the skin of chickens, and promptly produced a tumour. "But if the tissues receiving the injection contain leucocytes and their juices, they become much more susceptible to Rous agent." Rous sarcoma reduces one side of the problem to its simplest form, because this tumour can be transmitted by a cell free filtrate. The leucocytes include the lymphocytes, and the more nearly aseptic the foreign body the more numerous are the lymphocytes, so that the tissue culture experiments reinforce the histological evidence as to the part played by these cells, while the bacteria, the helminths and X ray burns referred to are all associated with lymphocytes rather than with polymorphonuclear cells.

An Attempted Reconciliation.

Turning back to my description of the inoculated mice, I would ask the reader to keep clearly before his mind the possibility that the early and late appearances of the lymphocytes are somewhat different phenomena, and they may indicate a response to different stimuli.

1. In my mice they begin as the response to the tubercle bacilli in any spot to which the bacilli have been carried by the wandering polymorphonuclear cells. As the spleen is the main depot for the organisms, the neighbouring fatty tissue is a characteristic spot. The infiltration may be traced by way of the omentum or mesentery or between the peritoneal surfaces of adjoining organs. The lines of cells develop from the peritoneal cavity outwards, that is to say, from the serous through the muscular to the submucous coat of the stomach. The lymphocytes forming the cushion beneath the inward bulging of a papilloma have not been caused to assemble on account of the irritation of the incipient tumour, but they are the cause of the bulging. The cells infiltrating the lobules of the pancreas have not migrated thither because the alveoli were proliferating, but they arrived there before proliferation began. It was the bacilli that opened the campaign. That this is the sequence of events is rendered almost certain by the following schedule: Fifty mice inoculated with tubercle bacilli without exception exhibit varying degrees of lymphocytic infiltration. Enlarged glands have been found in thirty-two, marked infiltration of the pancreas in twenty-eight, adhesions between adjoining organs in forty, carcinoma of the pancreas in six. The tumour is not the first stage of the process and the infiltration the end product, but *vice versa*. Where a tumour graft is implanted, it acts as an aseptic foreign body and attracts the lymphocytes, and the more foreign it is in reference to the tissues

of the inoculated mouse, the greater the number of lymphocytes.⁽²¹⁾ Hence the appearances in spontaneous and implanted tumours probably have different explanations. The lymphocytes are first in the one, the tumours first in the other.

2. In the mouse, many of the collections of lymphoid cells which we call glands apparently arise from small collections of these cells, which we have seen in the fatty tissue (Figure II). As the sizes increase a pseudocapsule may be defined and such collections may attain the size of a large tumour without any elaboration of structure; trabeculae, lymph paths or division into cortex and medulla are not present. Perhaps the mouse comes under Schäfer's note:

The gland seems in section to be an almost uniform mass of lymphoid tissue. This is the case with most, if not all, of the lymphatic glands of some animals.⁽²²⁾

A malignant cell drifting along the lymph stream might come to rest at the junction of two paths in the areolar tissue, and the lymphocytes would probably be attracted and surround it, but the cell may continue to multiply. In this way, a "gland" containing a metastatic growth would be formed, but its method of formation would be different from what takes place in the metastases of human cancer, where the cell is arrested after reaching the interior of the gland. If this explanation is accepted, it will help Murphy out of a tight corner.

3. The change in the attitude of the lymphocytes after immunization has been accomplished, may be due to some change which this process has brought about in the relation of the tissues and the implant. The first graft has altered this relation in such a way that these cells are no longer attracted by the second graft, just as it is the polymorphonuclear cells and not the lymphocytes that are attracted by the areas of necrosis which form in the deeper parts of a tumour. Caspari pointed out in 1923 that all transplantable tissues rapidly exhibit such necrotic areas, in which the polymorphonuclear cells soon become abundant.

Other remarks pertinent to this review of the old controversy are, that much of the experimental work was done before the variable nature of the lymphatic system of the mouse and its response to chronic infectious diseases had been investigated; that results obtained with rats and other animals cannot be applied direct to the mouse; that mouse tumours can be divided into two groups, one of which confers immunity on the host and the other does not.⁽²³⁾

Thus there is still something to be said for the lymphocytes; they are more than disinterested spectators of the drama, although their full rôle in the production of malignant disease cannot yet be defined. They are also a good source of growth stimulating substances.

Having attempted to avoid the Scylla of regarding the lymphocytes only as a defensive mechanism, one must also steer clear of Charybdis, which excludes these cells from any share in the production of malignant disease. Stripped of technical terms, this theory states that in irritation cancers:

The drops of oil or tar cause the building up of a dense mass of cells by drawing the tissue cells towards them and away from the intercellular substances and blood vessels. The bacteria which cause cancer doubtless act in the same way, in that they cause the building up of a dense stagnant mass of cells but by a different means—they produce the cell mass by stimulating the cells of the tissue to proliferate without forming to any extent intercellular substance and blood vessels.⁽²⁴⁾

Here the end result is much the same as in my experiments, but the means to that end are totally different. My illustrations speak for themselves.

Recapitulating, we have been dealing with an example of reaction proliferation culminating in malignant changes in the pancreas. When these epithelial cells are surrounded by the plasma cells and fibroblasts which follow in the wake of the polymorphonuclear cells, they stagnate and fade away. Surrounded by lymphocytes, they proliferate, and this change may become self-supporting. This series of mice furnishes circumstantial evidence that the lymphocytes are implicated in the change.

The Lymphocytes and Irritation Cancers.

Using irritation in the sense that the irritant is known, there is a group of neoplasms which supplies further evidence of the activity of an unknown intermediary between the irritant and the change to malignant disease. Cumulative evidence, experimental in animals, clinical in men, points to the lymphocyte which is often a characteristic cell on the outskirts of the lesion. This is an expanding class of tumours, and the results of experimental work are directly comparable with the facts of human pathology. The same irritant is used, an analogous precancerous condition is often seen, and the same types of skin cancer may be the final result. It has been discovered that there is an optimum degree of irritation for each agent, and probably also for each animal, and that the optimum is seldom the maximum. For instance, tar, intense cold and oil of mustard will each produce epithelioma in mice, but in combination, tar being applied first and then one of the others, the resulting warts do not grow as rapidly nor become malignant so soon as those produced by tar alone. For these experiments the intensity of the irritation seems to have become too great.⁽²⁵⁾ Current literature supplies many instances in which a condition of the skin with lymphocytic infiltration occasionally becomes malignant when subjected to X rays or radium—both of which agents in certain doses provoke the lymphocytes. These cells are often mentioned on the reports of the hospital team at Bristol co-operating in the treatment of cancer. They note a lymphocytosis in the blood, and much lymphocytic activity in the marginal zone about the tumour, resulting in the steady development of fibrous adhesions. It is claimed that these changes correspond with the appearances seen in the retrogression of transplantable mouse carcinoma.⁽²⁶⁾

Malignant changes also supervene on old standing lymphocytic conditions without the intervention of any known additional irritant, as, for instance, on old scars of burns, on mild degrees of burns (Kangri cancer), on tuberculous lesions of bones or joints, and it is well recognized as a not infrequent

change in old syphilitic lesions in which the lymphocyte is the characteristic cell.

Referring back to the description of the lesions in the inoculated mice, it will be seen that similar series of changes in parts of the pancreas are associated with the presence of lymphocytes (i) without demonstrable tubercle bacilli, (ii) with the bacilli apart from obvious tumour, (iii) with tuberculoma, (iv) with carcinoma, (v) with mixed cell sarcoma, (vi) with lymphosarcoma. It is therefore probable that some general stimulus is at work which, after stimulating several adjacent cells, not necessarily of the same kind, concentrates on or is absorbed by a single type of cell. This phenomenon is also seen in tar cancer, where a crop of papillae usually forms, not in contact, but close together. One of these begins to grow rapidly and absorbs the others in succession. This change may not develop until after a latent period during which the irritation continues to act. It, therefore, probably involves some additional sequence beyond the simple outpouring of the lymphocytes.

Tuberculosis and the Lymphocyte.

Calmette gives the following summary of the changes in the blood picture in man.⁽²⁷⁾ In incipient tuberculosis without a rise of temperature the number of polymorphonuclear cells is normal or diminished and the lymphocytes increased. As this early invasion slowly and quietly involves the lungs and lymph glands, the formula of resistance is developed. This consists of a moderate leucocytosis derived mainly from the increase in the lymphocytes. This changes to the formula of defence in cases of massive and highly virulent infection—great increase in the white corpuscles especially the polymorphonuclear cells with the appearance of large mononuclear cells and constant diminution of the lymphocytes. Finally, in open tuberculosis marked by cavity formation and very extensive caseation, the white corpuscles are from twice to three times as numerous as normal (16,000 to 20,000 per cubic millimetre), of which the polymorphonuclear cells constitute 90%. The lymphocytes as well as the medium and large mononuclear cells disappear and the latter are often found broken up and degenerated. This is the formula of defeat.

The formula of defeat, taken in conjunction with my experimental results, explains the antagonism of phthisis and cancer. The lung with cavities is practically a complicated internal ulcerating surface. The polymorphonuclear cells are in command and the quality in the growth stimulating substances necessary to produce malignant proliferation is absent.

Ninety years ago, Walshe,⁽²⁸⁾ the pathologist to University College Hospital, stated that "tubercle and cancer possess a sort of repulsion in respect of each other." He found only seven cases of active phthisis in 104 autopsies in cases of cancer. This antagonism was emphasized by Rokitsansky of Vienna in 1852,⁽²⁹⁾ and henceforth the coexistence of the two diseases was looked upon by most pathologists as the exception which proved the rule. In 1929, Raymond Pearl⁽³⁰⁾ published the evidence

obtained from the records of the Johns Hopkins Hospital, and after providing for a rigid system of controls in the selection of the cases, he confirmed the findings of the older pathologists, establishing the fact that only 7% of those dying of cancer had active tuberculosis, and conversely that those dying of phthisis very seldom had a tumour. On the other hand, evidence of healed or obsolete tuberculosis was just as common in cancer cases as it was in those dying of other diseases.

In 1924⁽³²⁾ from an analysis of the deaths in the occupations at the three census periods I showed: (i) That the incidence of cancer in nearly all the large occupations in 1911 was proportional to the incidence of phthisis in the same occupations in 1891; (ii) that the increase of deaths from cancer cannot be explained by the increase in the number of men who attain the age of fifty-five. The question of the accuracy of diagnosis is not involved in these results because the death certificates were all filled in at the one census period and any correction would shift all the numbers in the same direction.

The survivors in occupations which had been ravaged with phthisis in the age periods 25 to 34 and 35 to 44 would have been exposed to the same risk of infection as their dead *confrères* and these are probably the men who die of cancer. Their blood picture has regained the formula of resistance which includes the full activity of the lymphocytes. From other lines of evidence I consider it probable that the onset of cancer is determined by a fresh invasion by the tubercle bacillus.⁽³⁾

Bullock and Curtis⁽³¹⁾ have been producing cancer in rats by infecting them with the hydatid stage of the tape-worm of the cat. Of these tumours, 2,450 were in the liver, and 489 in other parts of the body. They remark that these rats often die with a chronic bronchopneumonia, "yet in spite of this condition primary neoplasms of the lung are very rare." Only four were found in the 489 tumours. They notice that epithelial tumours of the uterus were rather common and were associated with chronic suppuration, a condition which may have been antecedent or subsequent to the tumour; the authors suggest that it "was probably an etiological factor." That the correlation of the polymorphonuclear cells with the absence of malignant disease is more than a chance coincidence is confirmed by clinical facts. Septic conditions very rarely run into malignancy, and extremely few injuries received in the War have resulted in cancer. Those which have done so are mostly injuries to bones which were not followed by suppuration. Old standing ulcers and sinuses connected with bone seldom become malignant and the same holds good of papillomata, for even exuberant condylomata which are often moistened with pus rarely change into epitheliomata. A simple crack about the lips is undoubtedly more formidable than a corn on the foot, but it must be remembered that the former may intercept tubercle bacilli from food or other sources. The function of the polymorphonuclear cells is to prepare the tissues for repair and they do not often overshoot this mark. These characteristics of the polymorphonuclear cells fall

in line with one of the essential requirements in the evolution of animal life. In starvation, fat and the less important replaceable tissues are used up first, and we have seen that these cells are more resistant to deficiency of vitamins than the lymphocytes. Their functions are limited by the needs of survival. Their chief function is to get rid of dangerous invaders, especially bacteria. Chronic suppuration in man may cause lardaceous degeneration of the muscles, liver and other organs of the greatest importance to the organism, because the interests of all other tissues must be sacrificed in order to keep up the supply of these cells when they are the last barrier between life and death. But if they produced growth stimulating substances capable of carrying the process of repair into that of neoplasia, the victor in many a fight would have died of cancer and the qualities which made him the victor would be lost to the species.

SUMMARY.

This paper describes two conditions affecting the same part of the body in one hundred mice. One half of the animals had a polymorphic and the other half a lymphocytic infiltration of the pancreas. The former was associated with atrophy of the lobules and disappearance of the epithelial cells; the latter with a tendency to proliferation leading in six instances to carcinoma of the pancreas. From the discussion, it is concluded:

(1) That the lymphocytes take an active share in the production of malignant disease, and are an essential link between the normal and malignant cell.

(2) That prolonged suppuration in man affords protection against malignant changes—local as in chronic ulcers, general as in chronic phthisis—by its action in reducing the number of lymphocytes in the blood.

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(27) A. Calmette: "Tuberculosis in Man and Animals," 1923, page 248.

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(29) Rokitsansky: "Handbook of Pathology," 1852.

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(31) F. D. Bullock and M. R. Curtis: "Spontaneous Tumours of the Rat," *Journal of Cancer Research*, 1930, Volume XIV, page 1.

Legends to Illustrations.

- Figure I \times 100. Cells surrounding masses of tubercle bacilli in and near a small vein.
- Figure II \times 80. Lymphocyte infiltration between lymph gland and pancreas.
- Figure III \times 200. Proliferating pancreatic alveoli cells and ducts infiltrated with lymphocytes.
- Figure IV \times 200. Pancreatic alveoli proliferating and closing their ranks.
- Figure V \times 200. Precancerous proliferation affecting many adjoining lobules.
- Figure VI \times 400. *Carcinoma simplex* (negative retouched).
- Figure VII \times 200. Scirrhus carcinoma. Areas of malignant pancreatic cells and masses of lymphocytes adherent to colon.
- Figure VIII \times 120. Alveoli and ducts embedded in an early adhesion with hemorrhage. Polymorphonuclear reaction.
- Figure IX \times 320. Polymorphic infiltration and early organization separating pancreatic lobules.
- Figure X \times 750. Types of cells and commencing organization at an adhesion.
- Figure XI \times 750. Details of clusters of nuclei "mulberries and rosettes."
- Figure XII \times 320. Separated alveoli disappearing in an adhesion.

A LABORATORY INVESTIGATION FOR THE DETECTION OF TYPHOID CARRIERS.

By R. Y. MATHEW, M.B., B.S.,
Commonwealth Health Laboratory,
Toowoomba.

DURING the second week of February, 1930, two cases of sickness in Ward 2 of the Mental Hospital, Willowburn, were definitely diagnosed as typhoid fever. As this disease occurs very rarely in the hospital and as there had been a case in this ward

eighteen months previously, it was thought that possibly there was a carrier in this particular ward.

Arrangements were therefore made by Dr. J. E. F. McDonald, Medical Superintendent of the Hospital, with the Commonwealth Laboratory, Toowoomba, for an investigation of the occupants of the ward.

Nature of the Investigation.

Ward 2 contained 86 female patients of various ages and mental states. Their length of stay in Ward 2 and in the hospital ranged from three weeks to twenty-seven years. As no personal information of value in indicating likely carriers was procurable, it was decided to culture specimens of faeces and urine from all the patients in the ward and to search for organisms of the typhoid-paratyphoid and dysentery groups.

The examinations were begun on February 17, 1930, and completed on March 5, 1930. One typhoid carrier was found. Later on, cases in both sexes occurred in Wards C, D, B and 4; investigations were therefore continued until June 16, 1930.

Collection of Specimens.

The collection and transport of specimens to the laboratory were arranged by the hospital staff. Suitable containers were provided by the laboratory. Considerable difficulty was experienced in obtaining stools for examination, isolation of the patient for two days being required in some instances.

Loose motions were uncommon, in spite of saline purges, and, though most of the stools received were soft, some consisted of hard globular masses which were rather unsuitable for cultural purposes. The most frequent time of collection was about 5 a.m., the specimens remaining at room temperature until dispatched in batches to the laboratory. The specimens generally arrived at the laboratory, which is distant three and a half miles from the hospital, between 10.30 a.m. and 11.30 a.m.

Examination of Specimens.

On arrival at the laboratory the stools were emulsified in nutrient broth and left on the bench for about one hour. Inoculations of the faecal emulsions and of the urines were then made on MacConkey's plates. The plates were incubated at 37° C. and examined for non-lactose fermenting colonies after twenty-four hours and again after forty-eight hours' incubation. Suspicious-looking colonies were picked off and transferred to agar slopes, broth tubes and sugar fermentation tubes containing mannite. When the mannite was fermented with acid or acid and gas, an emulsion was made from the growth on the agar slope and agglutination tests were carried out against agglutinating sera of *Bacillus typhosus*, *Bacillus paratyphosus* A and B, *Bacillus dysenteriae* Flexner and *Bacillus dysenteriae* Y. When no change was observed in the mannite tubes agglutination tests were tried against *Bacillus dysenteriae* Shiga serum. The tubes were incubated in a water bath maintained at 55° C.,

readings of agglutinations being made after two hours in the case of the typhoid group and after four hours in the case of the dysentery group. Motility tests were performed with the broth cultures. The MacConkey's medium, mannite solution, agglutinating sera and standardized bacterial emulsions were supplied by the Commonwealth Serum Laboratories.

Particulars of the Cases of Typhoid Fever.

The particulars of the patients affected with typhoid fever are set out in Table I.

TABLE I.
Showing Particulars of Patients suffering from Typhoid Fever.

Case No.	Sex.	Ward.	Patients in Ward.	Widal Reaction.	Dilution.	Result.
1	F.	2	86	Positive 10/2/30	1 320	Died.
2	F.	2	86	Positive 10/2/30	1 160	Recovered.
3	M.	C	93	Positive 7/3/30	1 80	"
4	M.	D	99	Positive 7/3/30	1 80	"
5	M.	B	94	No reaction 31/3/30 Positive 9/4/30	1 320	"
6	F.	4	92	Positive 28/4/30	1 80	"
7	M.	C	93	Positive 30/5/30	1 80	"

One patient died; in three (numbers 2, 5 and 7) the disease ran a characteristic course to recovery; the remainder (numbers 3, 4 and 6) suffered from a mild type of the disease. Patient number 7 was a man sometimes engaged in working on the septic tank and filter beds.

Results of Examination and Details Regarding the Carrier.

Single specimens of faeces and urine were examined from all the patients in Wards B, D, 4 and 2, and two specimens were examined from all the patients in Ward C. In addition, single specimens from all the kitchen workers (male and female) and the milkers (male) were examined. Organisms of the typhoid-paratyphoid or dysentery groups were not isolated from the faeces of any save one. The exception was E.J.B., a female patient, aged sixty years, who had lived in the hospital for many years and in Ward 2 for eighteen months. From her faeces *Bacillus typhosus* was isolated on February 27, 1930. She has been in isolation in the hospital since that date. Prior to isolation she was at times violently maniacal.

No history suggesting that she had ever had typhoid fever or been associated with typhoid sufferers or carriers was obtainable. The results of examinations are set out in Table II.

The sequel is of interest. On October 28, 1930, with the object of removing a possible focus in the

TABLE II.
Showing Results of Investigation of Carrier E.J.B.

Date.	Specimen.	Non-Lactose-Fermenting Colonies on MacConkey's Medium.	Mannite.	Motility.	Agglutination Tests.
27/2/30	Fæces	+	A	+	<i>B. typhosus</i> serum 1/1280.
	Urine	—			
7/3/30	Blood Serum				<i>B. typhosus</i> emulsion 1/160.
9/7/30	Fæces	+	A	+	<i>B. typhosus</i> serum 1/1280.
	Urine	+	A	+	<i>B. typhosus</i> serum 1/1280.
24/9/30	Fæces	+	A	+	<i>B. typhosus</i> serum 1/1280.
	Urine (Catheter Specimen)	—			
29/9/30	Urine (Catheter Specimen)	—			

gall bladder, an operation was performed on the carrier, E.J.B., at the Toowoomba General Hospital by Dr. Aeneas McDonnell. Portion of the small bowel was examined, but no evidence of ulceration or scarring was found. The gall bladder was greatly enlarged and its colour was rather duller than the bluish colour of the healthy viscus. It was removed. There were slight thickening and evidence of inflammatory changes in the wall. The contents were pale, clear, viscid bile, a small amount of yellowish sediment, and one small bile-stained stone. From the bile a heavy growth of a pure culture of *Bacillus typhosus* was obtained. From the time of removal of the gall bladder until February 24, 1931, *Bacillus typhosus* has not been isolated in seven periodical examinations of the stools and urine.

Summary and Conclusions.

1. During four months (February, 1930, to May, 1930) seven cases of typhoid fever occurred amongst 464 patients (male and female) occupying five wards in a mental hospital of 1,100 patients distributed in twelve wards.
2. An investigation was made of the occupants of the wards concerned and of the kitchen hands and milkers for the detection of possible carriers. One carrier was found.
3. At subsequent operation inflammatory changes in the gall bladder were revealed; from the bile a pure culture of *Bacillus typhosus* was secured.
4. It seems reasonably probable that the carrier, E.J.B., was the direct source of infection of the two patients (patient number 1, who died, and patient number 2, whose illness followed a characteristic typhoid course) in Ward 2. At the time the cases occurred the pan system was in operation in Ward 2, but it has since been replaced by the septic tank system. It seems possible that patient number 7, who suffered from typical typhoid fever, obtained the infection indirectly while working on the septic tank and filter beds. No satisfactory explanation of the sources of infection in the characteristic case 5 in Ward B or in the three mild cases, 3, 4 and 6, in Wards C, D and 4 respectively, is made clear.

5. Dysentery occurs among the patients, but if any dysentery organisms were present in the stools examined, the delay between the evacuation and examination of the stools was apparently too great to allow viable organisms to be obtained.

Acknowledgements.

I wish to acknowledge the kindness of Dr. J. E. F. McDonald in permitting the publication of this report and the valuable assistance of Mr. C. L. Biggs in connexion with the examinations.

Reports of Cases.

UNUSUAL MANIFESTATIONS OF HYDATID DISEASE.

By ALAN E. LEE, M.D. (Melbourne), F.R.C.S. (England),
Honorary Surgeon to Out-Patients, Brisbane Hospital.

W.R.B., a male, aged forty-five years, was admitted to a surgical ward in the Brisbane Hospital at 2 a.m. on January 26, 1930. Eight hours before admission he had been seized suddenly with an agonizing pain in the upper part of the abdomen, so severe as to prostrate him. This pain had spread over the whole abdomen and remained severe up to the time of his admission to hospital. For nine years previously he had suffered intermittently from attacks of "indigestion," a pain coming on usually one and a half hours after meals. The attacks were of three to four weeks' duration and there were several months' complete intermission of symptoms between attacks. Recently he had noticed that the period between attacks was lessening. He had the typical appearances of a person suffering from an intraabdominal perforation. He lay immobile with knees drawn up. The rigidity of the abdominal wall was board-like. The obvious diagnosis was a gastric perforation. Operation was performed forthwith.

Operation.

When the abdomen was opened, much free, straw-coloured fluid was encountered. A perforation 0.25 centimetre in diameter was found on the anterior surface of the pylorus, one centimetre to the gastric side of the pyloric vein. It was surrounded by an area of induration and oedema three centimetres in width. The perforation was closed by oversewing the stomach wall with interrupted catgut sutures and reinforcing the closure with omentum. Further abdominal exploration revealed the following conditions.

Lying in the gastro-hepatic omentum, snugly fitting into the curve of the right margin of the stomach, was a cystic tumour, eight centimetres in diameter, apparently

ILLUSTRATIONS TO THE ARTICLE BY DR. THOMAS CHERRY.

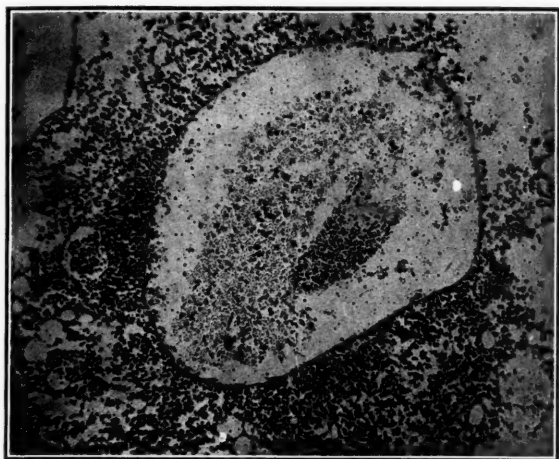


FIGURE I.

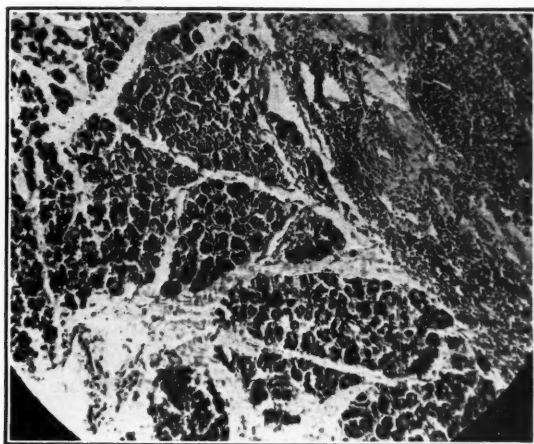


FIGURE II.

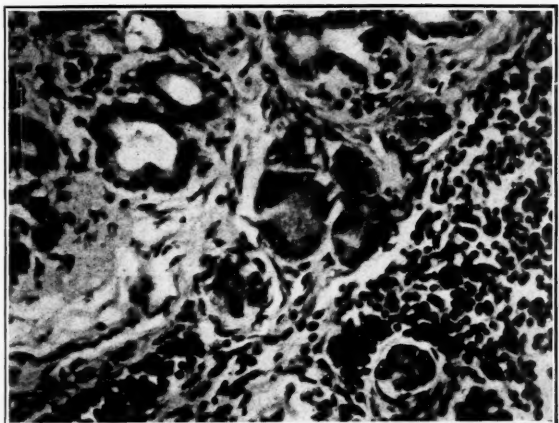


FIGURE III.

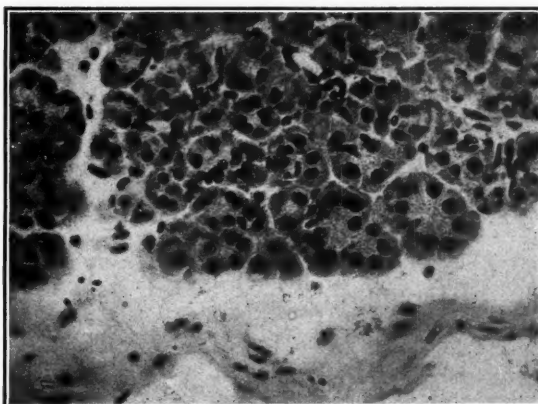


FIGURE IV.

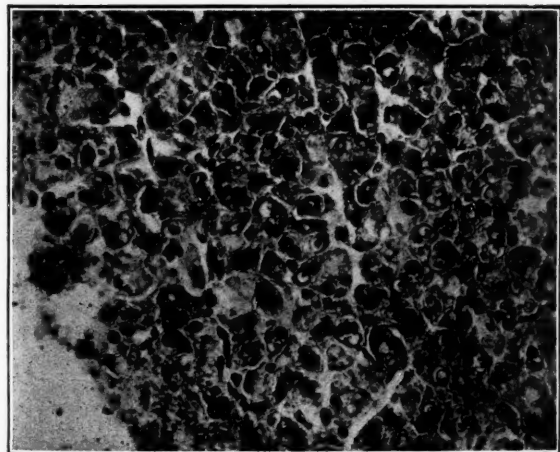


FIGURE V.

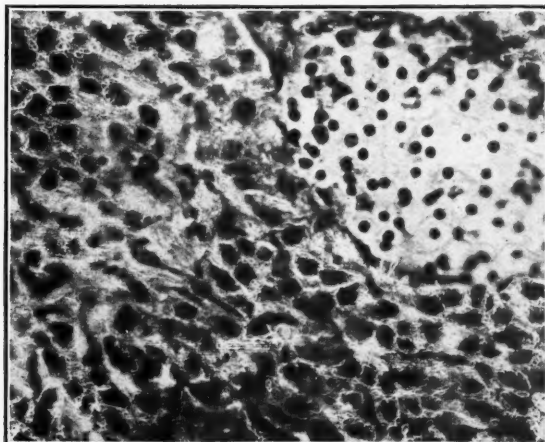


FIGURE VI.

ILLUSTRATIONS TO THE ARTICLE BY DR. THOMAS CHERRY.



FIGURE VII.

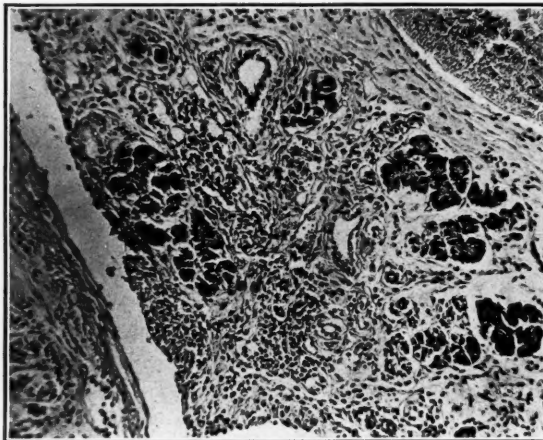


FIGURE VIII.

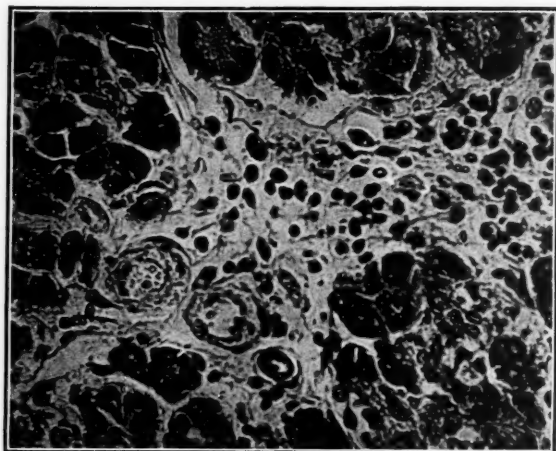


FIGURE IX.

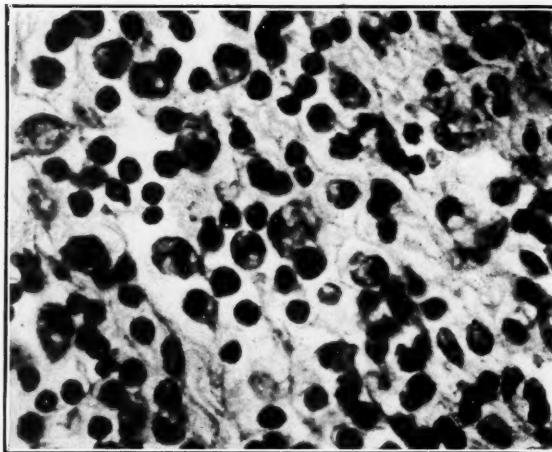


FIGURE X.

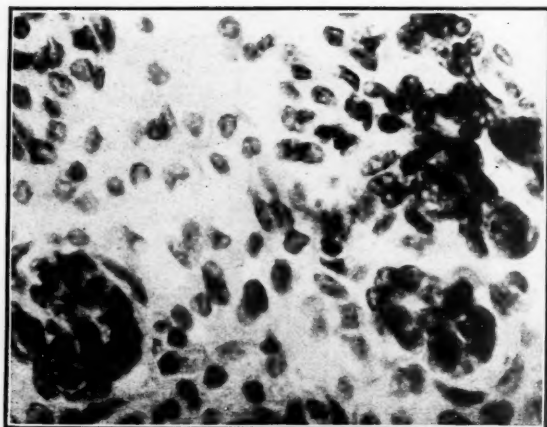


FIGURE XI.

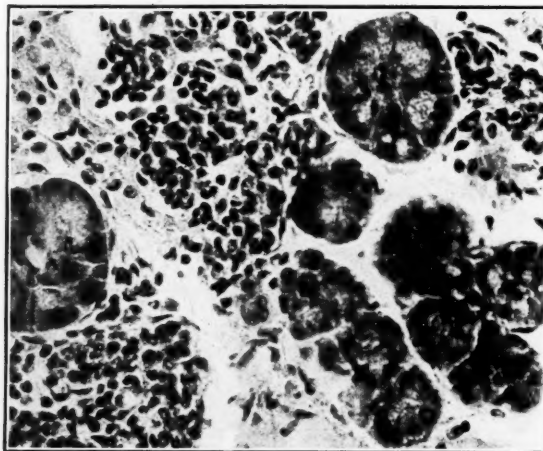


FIGURE XII.

attached to the stomach. To the right of this, in the gastro-hepatic omentum and below the pylorus, there were numerous greyish solid masses which had an average diameter of three centimetres. They extended upwards in a chain in the right margin of the ligament to the liver, where they terminated in a large "splash" of what was apparently grey carcinoma on the lower surface of the left lobe. The whole condition had the typical appearances of an extensive glandular and hepatic metastasis from, presumably, a pyloric carcinoma which had also ulcerated into the free abdominal cavity.

As the patient's condition was satisfactory and as exploration with a needle revealed the existence of clear watery fluid in the larger cystic tumour, this cyst was dissected out from the gastro-hepatic ligament and the stomach wall, to which it was loosely attached. The opportunity was also taken to dissect out and preserve a typical example of the "malignant glands" present between the stomach and liver. A drainage tube was then passed into the pelvis through a suprapubic stab wound and the main parietal incision completely closed.

The patient made an uneventful recovery and was discharged on February 26, 1930.

Laboratory Investigations.

The pathological findings were as follows:

1. The large cyst was a multilocular cyst with a hyaline lining membrane and containing clear watery fluid. Section did not reveal the nature of the cyst wall, which was structureless and non-staining.

2. The centrifuged sediment of the cystic fluid contained no *scotices* nor hooklets. No free hydrochloric acid was present.

3. The "glandular" mass may have been a gland; by macroscopic examination of a section it was observed to consist of a very tough adventitia enclosing a multilocular cyst.

The hydatid complement fixation test resulted in a "++++" reaction.

The red blood cells numbered 4,070,000 per cubic millimetre, the haemoglobin was estimated at 80%, the colour index was 1.0, the white blood cells numbered 14,200 per cubic millimetre. Polymorphonuclear leucocytes were in the proportion of 84%, large mononuclear cells 1%, lymphocytes 12% and eosinophile cells 3%.

Condition Some Months Later.

On December 12, 1930, in response to a letter of inquiry, the patient presented himself for examination. He was at this time perfectly well; he had had no dyspeptic symptoms since the operation and his weight had steadily increased during the year. Examination of the abdomen revealed no abnormality save the presence of two well healed scars.

Inquiry as to the man's previous life history elicited that he was born on the New South Wales side of the Queensland border and had never travelled further south than Glen Innes. In his youth he had driven many times between Glen Innes and Inverell and had often obtained drinking water from streams along the way.

Comment.

The freedom from symptoms persisting for almost a year after the apparent discovery of an inoperable malignancy would seem to indicate definitely that the diagnosis was erroneous. Evidently the "malignant glands" along the lesser curvature of the stomach were all thick-walled, degenerated hydatid cysts, though the condition of the liver still remains inexplicable, as it did not remotely resemble hydatid disease.

I have asked several surgeons who have had great experience of this disease whether they have ever seen a condition of abdominal hydatid disease which could be mistaken for abdominal malignant glands, and I have invariably had a reply in the negative. It is for this reason that I have deemed this case of sufficient interest for publication, although I recognize that the follow-up reports must continue much longer before finality can be reached in the diagnosis.

INTUSSUSCEPTION.

By CECIL UREN, M.B., Ch.M. (Sydney), F.R.C.S. (Edinburgh),

Proserpine, Queensland.

A FEMALE child, aged eleven months, was brought to me one Sunday morning with a history of slight diarrhoea for three days without blood or mucus in the stools. At 8.30 a.m. the child had a "fainting" turn, but no screaming. She quickly rallied and two other attacks occurred before 9 a.m. When I first saw her the child was crying lustily, causing the abdomen to be very tense, but in spite of this tenderness a large mass was palpable below the right costal margin. The upper border could not be defined and I erroneously considered the condition to be one of hepatic enlargement. There was no sign of collapse, the pulse was normal and the tongue moist, with a slight coating. The child was ordered an enema and a bismuth powder containing 0.008 gramme (one-eighth of a grain) of calomel.

I was away from town until 7 p.m., when I found that the returned enema material, which had been saved for inspection, was evenly blood-stained to a light red colour. The child had continued to take the fainting turns during the day at intervals of a quarter of an hour. The abdominal tumour was now much smaller, was sausage-shaped and there was a definite space between its upper border and the right costal margin. There was no sensation of emptiness when the right iliac region was palpated.

The child was taken to hospital and a colleague was called in. Operation was deferred on account of absence of collapse, the decrease in the size of the tumour, the absence of blood and mucus apart from that following the enema, and the absence of tenesmus. Nothing could be felt by rectal examination.

Half an hour later the tumour was considerably reduced by manipulation and the child then slept for two hours. When she awoke the bowels acted without undue straining and a fluid stool with some blood and a little mucus was the result. No tumour could be felt. An enema was given the following morning; the return was slightly blood-stained. The child was discharged from hospital on Tuesday morning none the worse for the ordeal.

Comment.

The case is of interest in that there was no definite sign or symptom of intussusception except the presence of a tumour. The typical screaming was absent. Mucus was extremely scanty and there was little bleeding. Between the fainting turns there was no collapse. As a tumour is not always palpable in cases of intussusception, how many cases of intussusception have passed unrecognized as such, being regarded as gastro-enteritis, even when the condition has had a fatal ending?

Reviews.

NORTH AMERICAN MOSQUITOES.

ROBERT MATHESON has produced a book that will be of value to those who work on North American mosquitoes, either systematically or from the public health point of view in North America.¹ His chapters on the structure and biology of mosquitoes and their relation to human welfare are exceedingly good. There are chapters dealing with the problem of mosquito reduction. He also gives notes on the collecting and preserving of mosquitoes and their larvae.

¹ "A Handbook of the Mosquitoes of North America; Their Structure, How They Live, How They Carry Disease, How They May Be Studied, How They May Be Controlled, How They May Be Identified," by Robert Matheson; 1929. London: Baillière, Tindall and Cox. Royal 8vo., pp. 285, with illustrations. Price: 25s. net.

The systematic portion is concerned with the common North American species of *Anopheles*, *Aedes*, *Culex*, *Theobaldia*, *Psorophora* et cetera, with keys to the species by adults, males and the larvæ.

The author, unfortunately, discards all subgeneric divisions. The arrangement of the genera and the species in the genera is arbitrary, and consequently does not show the relationship of the genera, nor of the species of a genus.

The illustrations are numerous and well prepared. The male hypopygia are exceedingly well portrayed. The figures of the entire larvæ are disappointing. Had larger figures of the head and the apex of the larva of the various species been given they would have been of much greater value.

It is difficult to forgive some of the numerous typographical errors. For example, the genus *Megarhinus* is spelt correctly in some sections (page 7), but in the section devoted to the genus (page 204) it is spelt *Megharinus*.

In the introductory discussion of mosquito reduction (pages 59, 60) the author writes: "The problem of mosquito reduction involves two distinct points of view: (i) that of the public health official who has been and still is largely concerned with the reduction of mosquito-borne diseases; (ii) that of the entomologist who urges that all species of mosquitoes be included in any plan of control." Surely the author does not mean this in the literal sense. No entomologist would urge, in a campaign against yellow fever, the control of the mosquito nuisance in addition to the destruction of the breeding places and the adult of the vector—*Aedes (Stegomyia) argenteus*. This would be a retrograde and very expensive step in regard to the extermination of a mosquito-borne disease.

HYDROLOGY.

HYDROLOGY, the employment of water as a medical remedy, has been in vogue since the first beginnings of medicine, and is still in use today. Its application is restricted to such remedies as fomentations, cold packs, baths, vapour baths and douches, so far as the general body of the profession is concerned, but in "The Physiological Principles of Hydrology" the joint authors, R. G. Gordon and F. G. Thomson, design to show that it has a wider range of usefulness and to explain its physiological action.¹

The book is one of a publication series issued under the title of the "Modern Treatment Series," the purpose of which is stated by the General Editor, Dr. F. G. Crookshank, to be "that the general practitioner should have the opportunity at his elbow or in his pocket and for a small price, of reliable guides to the present state of opinion and practice in some of the special branches of medicine and surgery."

This is a laudable and desirable object. It may be said of the best informed medical men, "there are more things in heaven and earth than are dreamed of in our philosophy," and possibly to scoff at and despise a remedy as quackery or a faith cure, may be to overlook something which, if used discreetly, would assist in practice.

The authors of the work under review set out on the task of explaining the uses of water as a healing remedy from the viewpoint of present day scientific beliefs. They are limited in space, which is possibly an advantage, as it makes for conciseness and brevity and saves the reader's time and possibly his patience. They do not pose as advocates, their intention being to show the purposes for which the remedy, whether it be as plain water or water containing chemical substances, is used and how such use may be physiologically justified.

In pursuit of this object the authors deal with the functions of the skin, with the circulatory and nervous systems, and with general metabolism, and point out the action of water, hot, cold, tepid and in combination with chemical substances, on the various parts to which they refer. Into a small space they have compressed a great deal of information, and the readers of their book will probably agree that there is greater scope for hydrology than as a foment to relieve pain or as a cleansing douche.

¹"The Physiological Principles of Hydrology," by R. G. Gordon, M.D., D.Sc., F.R.C.P., and F. G. Thomson, M.A., M.D., F.R.C.P.; 1930. London: Jonathan Cape; Sydney: Angus and Robertson. Crown 8vo., pp. 132. Price 5s. net.

In the last part of the book the authors mention and comment on the several complaints which are said to be benefited by hydrology. The work is of interest and should be of use to those who desire knowledge on the subject with which it deals.

MATERIA MEDICA AND THERAPEUTICS.

THE first edition of "A Treatise on Materia Medica and Therapeutics," by Rakhaladas Ghosh, was published in 1901. The twelfth edition is now to hand.¹ This is certainly one of the best text books on the subject in the British Empire and contains an amazing amount of information. As a text book for students and a work of reference for practitioners it can be confidently recommended. In the present edition many non-official preparations of doubtful utility have been deleted.

Amongst the new drugs incorporated in the present edition is sodium sulphocyanate, for arterial hypertension, its possible toxic effects being clearly indicated. Also sodium thiosulphate, the "hypo" of photographers. The author mentions this preparation as a remedy for arsenical poisoning, particularly the exfoliative dermatitis caused by organic arsenic preparations. No mention, however, is made of its use in bismuth or mercury poisoning, in which it is stated to be equally efficacious. Other additions are "Sanocrysin" (sodium aurothiosulphate), for pulmonary tuberculosis; "Novasurol" as a diuretic; "Tryparamide," a pentavalent organic arsenic preparation for trypanosomiasis and disseminated sclerosis, a preparation, however, as is pointed out, which may cause blindness or limitation of the field of vision; and "Stovarsol" and "Acetylarsan," which are also organic arsenic preparations for amebiasis, lamblasis and other conditions.

Among the newer local anesthetics described is "Butyn" (a "Novocain" derivative containing butyl and propanol in place of ethyl and ethanol, and with a toxicity equal to that of cocaine), also "Borocain" or ethocaine borate, which is neither toxic nor irritant. No mention is made of the newest local anesthetic, "Percain," a quinoline derivative. Ephedrine hydrochloride and synthetic ephedrine ("Ephetonin" of Merck) receive due consideration, as also does sodium tetraiodophenolphthalein ("Iodora" or "Opacin" or "Columbrin"), used in the diagnosis of gall bladder conditions. It is stated that intravenous injection of this preparation should only be resorted to when no results follow its oral use. "Plasmoquine" is described and its efficacy in the different forms of malaria indicated. A solution of quinine hydrochloride and urethane is stated to be the most suitable preparation for the injection treatment of varicose veins. Kurchi or Conessi bark is stated to be efficacious both in amebic and bacillary dysentery. "Cardiazol" (pentamethylene tetrazol), administered by mouth, subcutaneously or intravenously, is stated to act similarly to camphor and to be of value in the collapse of *angina pectoris*, myocarditis and circulatory insufficiency.

Serum treatment receives adequate consideration, except that no mention is made of serum treatment of measles, scarlet fever or infantile paralysis. The chapter on organotherapy should be read very carefully by the amazingly credulous present-day practitioner.

The chapter on radiation therapy has been rewritten and the untoward effects which may follow the application of ultra-violet rays are clearly set out. One rather serious mistake in the book must be pointed out. The author designates the pellagra preventive vitamin as F. This is quite wrong. The pellagra preventive vitamin is B₂ or G. Vitamin B₁ or F is the antineuritic vitamin. On page 577 cineol is described as a volatile oil. This is not correct. Cineol is not a volatile oil itself, but is a constituent of several. Again, the author uses the scientific designation N.O. (natural order) throughout where he should use the correct term "family." Some misprints occur, such as "paws" (page 272) for "yaws," and "oil, incompatibles of tannin" (page 617) should be "all incompatibles of tannin."

Apart from these few blemishes the work is admirable.

¹"A Treatise on Materia Medica and Therapeutics, Including Pharmacy, Dispensing, Pharmacology and Administration of Drugs," by Rakhaladas Ghosh; Twelfth Edition, by Brendra Nath Ghosh, F.R.F.P. & S.; 1930. Calcutta: Hilton and Company. Crown 8vo., pp. 775. Price: 12s. 6d. net.

The Medical Journal of Australia

SATURDAY, MARCH 7, 1931.

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CANCER AND PUBLIC HEALTH AUTHORITIES.

THE annual report of Sir George Newman, Chief Medical Officer of the Ministry of Health of Great Britain, always contains information that is most valuable to the student of preventive medicine. In his report for the year 1929, recently received, Sir George Newman points out that cancer in Great Britain accounts for 10.7% of the total number of deaths. The number of deaths attributed to cancer during the year was 56,896 equal to a death rate per million persons living of 1,437. This rate is higher than that recorded for any previous year. He refers to the widespread interest that has been aroused in the subject of cancer in medical circles and among the members of the community at large, and to the efforts that are being made to overcome it. He adds that, numerous and diverse as these activities are, there remains still another field which does not yet occupy what appears to be its proper position, this is the public health field. Coming as it does from one qualified to express an opinion on the subject, this statement demands careful consideration.

The first thing to be remembered in connexion with this question is that the cause of cancer is not known. In these circumstances the initiation of

satisfactory preventive measures by public health authorities or by any one else is not possible. Early recognition is the best that can be done. Even as far as the small group of cancers associated with certain occupations are concerned, little can be done beyond avoidance of contact as far as possible with the carcinogenic agent and regular inspection of those exposed to risk, so that precancerous and early cancerous lesions may be discovered as soon as they appear and be subjected to proper treatment. Sir George Newman is not concerned only with preventive measures, however. He refers to laboratory research into the question of causation, research connected with treatment, more precise appraisal of the results of treatment and wider provision for radiological treatment. He thinks that modification in the views held as to causation, the non-infectivity of the disease, better knowledge of the results of treatment and extension of the powers of public health authorities to provide treatment for the sick are likely to encourage and enable some authorities to play a more effective rôle in the study and control of cancer.

With the relationship of Sir George Newman to the public health authorities mentioned by him and with effect likely to be produced by his statements we are not immediately concerned. We are concerned with the responsibility of the health authority and the government controlling the authority and its attitude to the study and control of cancer. In Australia the Commonwealth Government has done something in regard to the provision of radium and its use in treatment of malignant disease. State Governments have done very little. Neither Commonwealth nor State Governments have devoted themselves to cancer research. It may also be asked whether both Commonwealth and States could not do more in the education of the public in regard to the known facts of malignant disease. We do not propose to discuss these aspects, important though they be, but would draw attention to the need for activity in another direction. As already stated, early recognition of cancerous lesions is the one factor that will help to reduce cancer mortality. Even the most stupid politician would, it may be presumed, agree that a cancer cannot be skilfully treated until it

is known to exist. Diagnosis may be extremely difficult. The best informed medical practitioner, skilled in diagnostic methods and equipped with the latest appliances, may, as pointed out recently in these pages in reference to cancer of the stomach, be unable to determine the presence of suspected malignant disease. How, then, can a non-medical person discover malignant disease and treat it? The Medical Acts in the several States do not prevent the treatment of malignant disease by charlatans. The *Medical Practitioners' Registration Ordinance*, 1930, recently introduced in the Federal Capital Territory, states that a person other than a registered medical practitioner, shall not "give or perform, for fee or reward, any medical or surgical service, attendance, operation or advice" and exacts a large penalty from a convicted person. All medical practitioners can point to unfortunate persons who have been robbed of their only chance of successful treatment by the flamboyant claims of a quack or the psychological attention of a faith healer. The State intervenes when a person is subjected to bodily violence or when he is deprived of his property by theft, yet it does nothing when he is hastened to his death by money-making charlatans. It is high time that the State Governments turned their attention to this matter. Until this is done it is rank hypocrisy for them to pretend to be interested in reduction of mortality from cancer.

Current Comment.

OSTEOMYELITIS.

THOUGH authorities are at variance regarding the exact mode of procedure in the treatment of osteomyelitis, there is one principle, the provision of drainage of the infected area, which is common to all methods; it is the principle on which practically every method is based. The stage at which active measures of treatment should be instituted, the extent to which the marrow cavity should be laid open, the treatment before and after operation, all give rise to disagreement. Radicalism vies with conservatism. At a meeting of the New South Wales Branch of the British Medical Association in October, 1928, Wade expressed the opinion that efficient drainage for early acute osteomyelitis could be obtained by laying bare the bone and drilling into the marrow. At the same meeting

Vickers stressed the necessity for gouging away the bone and laying bare the marrow cavity for the whole extent of the disease process; Royle advocated the application of diathermy when the condition was recognized at a very early stage. By some surgeons in other parts of the world the rather terrifying operation of diaphysectomy is recommended. Thus it may be seen how widely divergent the views of authorities may be. Of course, a record of the various lotions and antiseptics which have been recommended for use in the treatment of osteomyelitis would occupy a volume of moderate size.

In 1927 H. W. Orr devised a method for the treatment of acute and chronic osteomyelitis; he also applied the method in the care of compound fractures. His views, no doubt, came as a shock to the dyed-in-the-wool conservatives in surgery and, in regard to acute osteomyelitis, they still appear rather startling. Briefly put, Orr's method is as follows: An incision is made of sufficient length to allow free access to the diseased area. The bone is chiselled away so that all dead bone is removed and there is no bone overhanging any diseased tissue. The diseased area is cleaned out; damage is avoided, as far as possible, to healthy tissues and to tissues undergoing repair. The wound is then dried, swabbed out with a 10% tincture of iodine and 95% alcohol. The entire wound is lightly packed with gauze soaked in soft paraffin and a bandage is applied. The limb is placed in a sound anatomical position and immobilized in a plaster bandage, preferably, or a suitable splint. The plaster is not split nor is a window cut in it. If the temperature should rise unduly or if other signs of acute sepsis should ensue, the plaster is removed and the wound dressed, otherwise no dressing is done until the odour becomes offensive. In many instances it is unnecessary to change the dressing for several weeks.

Irvin E. Deibert has recently published his results from the treatment of 100 patients by Orr's method.¹ Before undertaking this investigation Deibert had been accustomed to using Dakin's treatment. He makes no comparison between the results obtained with Orr's method and any other method, as he recognizes that numerous factors apart from treatment are involved. The age of the patient, the bone and the particular portion of it affected, the virulence of the invading organism, the duration of the illness and the individual resistance, all would have to be taken into account.

Of 37 patients suffering from acute osteomyelitis, six died. These six were children who were extremely ill or moribund at the time of their admission to hospital; from the blood of each a culture of *Staphylococcus aureus* was made. No other deaths occurred in the series. The temperature and pulse rate of the patients affected with acute osteomyelitis reached normal within an average period of five days. The patients were usually free of pain the day following operation. Deibert remarks that

¹ *Annals of Surgery*, December, 1930.

the comfort of the patients was a striking feature; he suggests that if for no other reason than this the Orr method is preferable to any other. In no instance was it found necessary to change the dressing before the elapse of three weeks; in many instances it was possible to allow the limb to remain undisturbed for six weeks. As a rule, when the dressing was first changed, the wound was found to be bathed in pus and filled with healthy granulation tissue. In six instances the wound was almost completely healed when the original dressing was removed at the end of a period of six weeks. Cure of acute osteomyelitis was effected after one to five dressings had been applied; cure of chronic osteomyelitis resulted, as a rule, after the application of one to three dressings.

Deibert discusses the advisability of immobilizing the joints when the disease has reached a chronic stage. As a result of his observations he concludes that there is no danger of ankylosis unless the infection has definitely invaded the joints.

Six patients suffering from compound fractures were treated by the Orr method. An important procedure in dealing with these fractures, in addition to the usual cleaning up process, is the removal of all loose fragments of bone. Extension, when it was necessary, was carried out by means of Steinman's pins or ice tongs; the plaster splint was applied while the extension apparatus was in position.

Deibert claims that his results justify the use of the Orr treatment. The wounds healed rapidly, there was a minimum of sequestration and the orthopaedic results were satisfactory. Economically, an advantage of the treatment is that a prolonged stay in hospital is usually unnecessary. Attention is required at such infrequent intervals that the surgeon may insure asepsis by himself carrying out the necessary dressings. This is a definite advantage; it is generally impracticable when any other method is employed.

Good results might reasonably be expected from the Orr method of treating chronic osteomyelitis, for in this stage of the disease the abscess is walled off, there is no advancing sepsis, and, though necrosis is still taking place, the process is one mainly of repair rather than destruction. Rest and removal of dead tissue only are required in order that facilities may be provided for the continuance of Nature's work of reconstruction. But caution should be observed before the method is applied either to the treatment of acute osteomyelitis or compound fracture. It scarcely seems logical treatment to shut in an area of acute sepsis, for, however careful the surgeon may be or however ruthless, he cannot be certain that he has removed the whole of the septic material; furthermore, it must be remembered that operation does not afford relief to any blood infection which may exist. Again, the method entails the destruction of a considerable amount of bony tissue, whatever the stage of the disease process; this will find disfavour with those surgeons who believe only in the removal of bone

which is surely dead. In the treatment of compound fractures all are agreed on the necessity for the removal of dirt and injured tissue, but no surgeon can be sure that he has made the wound scrupulously clean, nor can he be certain that anaerobic organisms are not lurking in some of the dark corners. To close such a wound seems to invite trouble. True, Orr does not suture the wound, but he sets up a moderately efficient barrier to the ingress of oxygen. In the treatment of both acute osteomyelitis and compound fracture no doubt many splendid results may be obtained by the use of Orr's methods, but there seems to be a possibility that these results may be obtained at the cost of a few limbs and a few lives which might have been saved by the employment of other methods.

SURGERY OF THE COLON AND VACCINATION.

ONE of the main complications to be feared after surgical operation on the colon is peritonitis. There are several reasons why peritonitis should occur more frequently after operations on the colon than after operations on other parts of the intestinal tract. One of the most important of these is the peculiar muscular arrangement of the colon; on account of the powerful peristaltic action strain on sutures may be severe, leakage is likely to occur and pathogenic microorganisms present in the lumen are given an opportunity of fulfilling their destiny. In a recent communication F. W. Rankin and J. A. Barga¹ draw attention to the inconstant blood supply of the large bowel and to the increased permeability of the large bowel under obstructive conditions. They "have a fixed idea" that manipulation of colonic growths with spreading of the colonic infection already present, is a greater source of potential danger than leakage at suture line. In support of this they record results of bacteriological investigations of eighteen malignant colonic lesions. From the subserosal tissue overlying the tumour and near the tumour green-producing streptococci and colon bacilli were grown in thirteen instances. They then give details of experiments on animals showing that a transient immunity may be produced by intraperitoneal vaccination and that this immunity will protect the animal against peritonitis. They further report on 222 patients subjected to operations on the colon and treated by intraperitoneal vaccination before operation. They compare these with 58 patients who were subjected to a similar type of operation and who received no vaccine. Among the former group eleven died and among the latter thirteen. With the vaccination other preliminary measures are used—bowel irrigation, correction of metabolic disorders and so forth. It is not stated whether these were used in the second group and no *post mortem* findings are recorded. In spite of this the report of Rankin and Barga (it is their second report) calls for careful study and the method for critical trial.

¹ *Archives of Surgery*, January, 1931.

Abstracts from Current Medical Literature.

PÆDIATRICS.

Measles Prophylaxis in Infants.

L. H. BARENBERG, J. M. LEWIS AND W. H. MESSER (*Journal of the American Medical Association*, July 9, 1930) have studied the comparative results with the use of adult blood, convalescent serum and immune goat serum (Tunnick) in the course of an epidemic in an institution containing 325 children, 150 of whom were under two years of age and the remainder from two to four months. The epidemic lasted two months; and of 318 susceptible children 132 or 42% developed the disease. Of 56 children actively exposed who received thirty cubic centimetres of adult whole blood, 43 contracted the disease. Of this group 64% were benefited by the injections and the disease assumed only an attenuated form. Attenuation occurred in 22 of 26 children in whom the blood was injected during the first five days of the incubation period. No mollification occurred, however, if the blood was given later than this. The modification produced by this means was not quite so pronounced as when convalescent measles serum was given. No complications occurred in the attenuated disease and the percentage for the whole group was eleven, as against thirty in a control series. The entire group of 38 children who received eight cubic centimetres of immune goat serum (Tunnick) developed typical measles in spite of the fact that 20 received the serum within the first three days of the incubation period. The percentage of complications in this group was as high as the controls. Of 13 children who received normal goat serum, 12 came down with typical measles, so no immunity was apparently confirmed by either forms of goat serum. Sixty children received six cubic centimetres of convalescent measles serum and 44 or 73% remained completely protected, while 14 or 23% developed attenuated measles without complications. The authors state that this latter is by far the best technique, but is limited because of its unavailability, when healthy adult blood is the best substitute.

Cirrhosis of the Liver.

ROBERT HUTCHISON AND S. L. SIMPSON (*Archives of Disease in Childhood*, June, 1930) record an instance of cirrhosis of the liver in a patient who had been first observed as a child of five years with a large, smooth liver as his only symptom. Two years later the organ was observed to be smaller and irregular, and after a further year had shrunk well above the costal margin with a just palpable spleen. His general health remained fairly good until he was twenty-eight years old (1929), when he complained of attacks of severe epigastric pain. He was then

thin and pallid, but had none of the other stigmata of cirrhosis. His liver was again below the ribs, hard, irregular and bossed. There was no ascites or splenomegaly and the Wassermann test gave no reaction. He died four days after laparotomy, at which three large rounded masses of white friable material were found overlying the stomach and attached to the lower surface of the liver. Autopsy examination of the liver showed it to be coarsely nodular with a polylobular fibrosis with scattered pure white nodules of new growth surrounding a large wedge of the same material, partly necrotic. The hepatic veins were abnormally wide and thick and the hepatic portion of the inferior vena cava was occluded by the pressure of a fibrous band and ended in a blind extremity; the only vein opening into the inferior vena cava was a relatively small one. Portal veins, bile ducts and gall bladder were normal, but the diaphragmatic veins were dilated. There was plain evidence of an attempt at a collateral venous circulation to compensate for the stenosis. The tumour cells were vacuolated and resembled hepatic cells. They consider that the growth was a primary carcinoma of the liver, as the cells in places formed tubules containing bile pigment and the growth was arranged in tubules similar to the pseudolobules of regeneration, from which it undoubtedly arose. The venous occlusion was found to be due to true thrombophlebitis and not to the growth, and had occluded the hepatic ostia long before death. Turnbull points out that if this occlusion is a complication of non-syphilitic cirrhosis of the liver, it is highly exceptional. The authors also present a review and summary of previous cases of occlusion from all causes, including five in which carcinoma supervened, and six cases appearing in childhood. Endophlebitis, thrombophlebitis, mechanical causes and congenital stenosis are discussed in the aetiology and they favour a gradual spreading thrombus formation as an explanation of the sudden attacks of abdominal pain and rapid hepatic enlargement. A congenital malformation is offered as the ultimate cause in their own and similar cases beginning so early in life.

Second Attacks of Poliomyelitis.

G. F. STILL (*Archives of Disease in Childhood*, October, 1930) records a case of recurrence of poliomyelitis in a girl aged seven years. The first attack occurred at one and three-quarter years and the residual paralysis was confined to the left leg. On the second occasion the right shoulder muscles were affected. The author reviews the alleged cases previously reported and selects eight instances showing satisfactory evidence of a true recurrence. Examination of these shows that the minimal duration of immunity is probably about two years. Recrudescences, however, may occur up to three months and a child may remain a carrier up to this time. In three of the eight cases an interval

of fourteen years elapsed. In one instance three definite and distinct attacks occurred. Of these exceptions the author writes: "This is no proof that such an attack does not confer . . . permanent immunity. Indeed it may be doubted whether any form of infection necessarily establishes permanent immunity."

Advanced Banti's Disease.

E. C. WARNER (*Proceedings of the Royal Society of Medicine*, August, 1930), following Pearce's suggestion of ligature of the splenic veins in Banti's disease, describes the successful treatment of a boy aged ten years. Physical signs consisted of ascites, a small, hard liver, enlargement of the spleen to the umbilicus, with many large, distended veins conducting blood upwards on the front of the chest and abdomen. Blood examination revealed a secondary anaemia and leucopenia, with a normal platelet and differential count. Lymphocytes were absent from the ascitic fluid. The Wassermann reaction was not obtained and leucocyte tolerance was very unsatisfactory. The boy was very drowsy and there was evidence of fluid accumulations in the pleural and pericardial sacs. Following a period of rest and glucose administration the boy improved enough for a laparotomy. The presence of hepatic cirrhosis was confirmed and the splenic veins were tied without difficulty, apart from some bleeding from the gastro-splenic omentum. Epistaxis and some small hæmatemeses occurred during the convalescence, which was rapid. Two months later the blood count and liver tolerance were normal and had remained normal up till the time the author wrote, ten months later. The liver and spleen remained the same size as before, but there was no reformation of fluid. Venous anastomoses had diminished and the boy was at work at school.

Treatment of Chorea by Milk Injection.

A. E. VIPOND (*Archives of Pediatrics*, October, 1930) relates his impressions after treatment of twenty-six choreics of all grades by milk injection. His technique is to inject five cubic centimetres of carefully sterilized milk into the thigh muscles every three days until improvement occurs. A leucocytosis follows and many patients are relieved after four to five injections. Some require as many as twenty. The patients with the more severe and acute chorea respond quickest. There are no complications and no alarm should be caused by a simple reddening of the skin over the site of injection.

Neurological Complications of Pertussis.

R. C. ELEY (*New England Journal of Medicine*, July, 1930) reports four cases of neurological sequelæ to pertussis, consisting of epilepsy, mental retardation, spastic paralysis, myelitis and visual disturbances, temporary and permanent. While admitting that gross hæmorrhage and minute hæmor-

rhages may occur into the brain during the course of the disease, he quotes authorities and *post mortem* evidence for a concomitant encephalitis, leading ultimately to neuronal degeneration or blocks in the fluid circulation. One of his epileptic patients showed calcified areas in the radiogram which may have been due to old hæmorrhages. Two had greatly dilated ventricles. The author pleads for a closer observation of the central nervous system during any acute systemic affection. Convulsions occurring in the course of pertussis should receive definite prognostic significance.

ORTHOPÆDIC SURGERY.

Stenosing Tendovaginitis.

H. FINKELSTEIN (*The Journal of Bone and Joint Surgery*, July, 1930) reviews the literature and discusses the aetiology, anatomy, pathology and experimental work, differential diagnosis and treatment of stenosing tendovaginitis at the radial styloid process. The tendon sheath is usually about twice the normal thickness, the tendons being thinned out at the point of constriction. They do not glide freely on movements of the thumb. In severe cases the sheath may be very greatly thickened and adhesions may exist between the tendon and the sheath. The most pathognomonic objective sign is excruciating pain on grasping the patient's thumb and quickly abducting the hand ulnarward. The diagnosis involves consideration of tuberculous tendo-vaginitis, tuberculous osteitis, *tendovaginitis crepitans*, periostitis, neuritis and arthritis, but is usually easy when one is fully acquainted with the symptoms. The treatment should be conservative in the acute stage, from which several authors have reported cures, and should consist of immobilization in a plaster cast, compression bandage or splint, baking, massage and diathermy. Operative treatment is indicated if relief is not obtained within a period of four weeks, and consists in splitting the sheath or removing the entire circumference of it, but the author favours the removal of the entire tendon sheath.

Cordotomy and Relief of Pain.

F. C. GRANT (*Annals of Surgery*, December, 1930) maintains that cordotomy has three distinct advantages over the other methods of relieving pain. A greater area of anaesthesia can be produced by section of the antero-lateral pathways than by any other means. Pain and temperature sensation alone are obliterated without involvement of touch or position sense and hence motor function remains unimpaired and the operative procedure requires only a small laminectomy and is, therefore, much less exhausting to debilitated patients. But cordotomy has the disadvantage that unless the incision into the cord is accurately placed, the pain may not

be completely relieved or the motor pathways may be damaged, resulting in paralysis of the legs and interference with sphincteric control. A distinct advance in the technique of cordotomy has recently been made following the discovery that section of the pain fibres in the cord causes the patient no distress. Manipulation of the posterior roots is painful, but curiously enough cutting into the antero-lateral tracts is not. Hence operation may be carried out under local anaesthesia or preferably nitrous oxide analgesia plus local anaesthesia, which holds the patient quiet until the adjacent posterior roots have been separated and the cord rotated ready for cordotomy. The reports quoted and the author's experience seem to suggest that the temperature fibres are located more centrally, while the pain fibres lie superficially over a larger surface area. If the incision is carried from exactly the plane of attachment of the dentate ligament forward to just beyond the level of the emergence of the anterior root, it need not penetrate to a greater depth than two and a half millimetres at any point. The author considers that cordotomy may be performed either unilaterally or bilaterally, depending on the extent of the pain. If the pain is referred to the bladder or rectum, or if it is caused by a rapidly spreading malignant tumour, the wiser course is to do a bilateral section. When both antero-lateral columns are to be cut, the incisions should not be made at the same level, but must be separated by at least one whole segment. In this way interference with the blood supply to the cord, possibly producing a transverse lesion, is avoided. The cord may be sectioned as high as the sixth cervical segment if necessary. Incision at a higher level may involve the phrenic distribution, causing respiratory embarrassment. The third or fourth thoracic segment is the point of election for cordotomy. In this region the vertebral curve brings the cord into a relatively superficial position, the cord is small and may be rotated easily, all possibility of diaphragmatic involvement is avoided and anaesthesia as high as the ensiform cartilage may be produced. The operative incision is made in the mid-line from the first to the fifth thoracic spines and the second, third and fourth spines and laminae are removed. It is important that the laminae be cut away with a rongeur as widely as possible, for the greater the lateral exposure, the more readily may the cord be rotated for section. After hæmostasis has been completed, the dura is carefully opened and retracted to either side with stay sutures.

Spring Back Brace for Fractured Clavicles.

H. W. SPIERS (*The Journal of Bone and Joint Surgery*, July, 1930) reports a spring back brace for fractured clavicles. It is somewhat like the Taylor brace, but the vertical bars are carried upward to well above the level of the acromion processes. Two

cross bars are placed, one at the top of the brace and one below the level of the axilla. Shoulder pad straps fixed to these bars pull the shoulder backwards and outwards. He claims to have secured exceptionally good results, even in comminuted fractures of the clavicle.

Streptococcal Infections of the Epiphyses and Short Bones.

D. B. PHEMISTER, A. BRUNSCHWIG AND L. DAY (*The Journal of the American Medical Association*, October 4, 1930) have conducted a bacteriological examination of tissue removed from six patients—two each suffering from Köhler's disease of the tarsal navicular, Legg-Perthes's disease and Klenbock's disease of the *lunatum*. They found streptococci present in four of the six specimens and suggest the possibility that streptococci play an important rôle in the aetiology of these diseases and that other factors may also bring them about.

Chronic Infectious Arthritis and Arthroplasty.

R. J. MROZ AND H. W. MEYERDING (*Proceedings of the Staff Meetings of the Mayo Clinic*, October 1, 1930) report a case in which practically every joint in the body was ankylosed. After two arthroplasties on each hip and an arthroplasty on each knee the patient was able to walk on crutches and swing his hips, but muscular atrophy had become so great during the previous illness that full recovery did not ensue. The authors claim, however, that this patient would otherwise have been totally and permanently disabled, whereas he is now able to walk and use his arm and is independent of help from others.

Surgical Tuberculosis of the Lower Extremity.

A. ROLLIER (*The Journal of Bone and Joint Surgery*, October, 1930) discusses conservative treatment in surgical tuberculosis of the lower extremity and maintains that the results still justify his practice. He claims to have obtained healing in various joints of the lower extremity without sacrificing mobility. He adopts the following standard of cure from a radiographic point of view: (i) Demarcation of a zone of sclerosis between the healthy tissues and the diseased tissues; (ii) absorption of abscesses, infiltrations, fungosities *et cetera*; (iii) reconstruction in the zone of atrophy and softening of a new bony substance with strong trabeculous meshwork; (iv) reorganization of sequestra, filling up of sequestra, filling up of cavities and of defects by connective tissue; (v) readaptation to functional demands by new joint formation. The author maintains that hip joints which have retained mobility show under this régime less tendency to recurrence than those which have become ankylosed. The diet should be composed above all of cereals, vegetables and fruit, and it is imperative to pay attention to the morale and the physique of the patient.

Special Articles on Diagnosis.

(Contributed by Request.)

XXXV.

TYPHOID FEVER.

OWING to the wide variation in the symptomatology and severity of typhoid fever a comprehensive dissertation on this subject would almost fill a number of THE MEDICAL JOURNAL OF AUSTRALIA. Therefore in this article an attempt will be made to select the salient features and to assess them at their proper worth.

The diagnosis may be a matter of great difficulty, both clinician and pathologist being at times unable to establish definite proof of invasion by the *Bacillus typhosus*, and there is no condition in which clinical experience is of greater value, as at times typhoid fever is imitated by many different diseases, and if it is not kept in mind cases will be overlooked.

Diagnostic data may be divided into clinical and bacteriological, and these will be dealt with in order.

Clinical Examination.

History: An accurate history is essential, for, although many patients state that the onset of their illness was sudden, careful questioning of the patient and relatives usually elicits the fact that prior to the onset there was a definite period of varying duration in which headache, lassitude, anorexia and malaise were present to a greater or less degree. Abrupt onset does undoubtedly occur, but it is rare.

Epistaxis: This is quoted in text books as a frequent and suggestive early symptom, but in the cases occurring in Brisbane it is the exception rather than the rule.

The Temperature: The temperature rises by steps, attaining a level of 39.4° to 40.5° C. (103° to 105° F.) by the fifth to the seventh day; frequently, however, the patient does not come under observation until this stage is reached, so the information given by early charting is lost. Once the fever has reached its maximum it usually maintains a characteristic uniform level, the daily remissions being often less than 0.25° C. (0.5° F.). Marked remissions should at once suggest the possibility of a wrong diagnosis or the onset of some complication. With regard to the latter it is interesting to note that pyelitis, which occurs in quite an appreciable number of cases, is frequently symptomless, no complaint being made of scalding or frequency. Microscopic examination of the urine should be carried out when any patient has a fever characterized by definite remissions.

The Pulse: The pulse is slow in comparison to the height of the fever; when dicrotic in addition, it is in itself almost diagnostic.

The Eruption: The classical rose spots are very scanty; careful inspection often fails to reveal their presence at various stages of the disease. Other small skin lesions may cause difficulty in identification and too great stress should not be laid on the presence or absence of a rash.

The Tongue: The tongue is dry and at first heavily coated with a white fur; later this becomes brown and, if the toxæmia is severe, may be almost black.

The Bowels: The bowels are usually loose, constipation being uncommon. The stools often assume the characteristic "pea soup" appearance within the first few days. Distension is not a feature; when present, it is generally an indication of severe toxæmia or faulty diet.

The Abdominal Reflexes: A sign which has proved remarkably constant in adults is absence of the superficial abdominal reflexes; in the opinion of the author this is a useful diagnostic sign. Early in the disease the reflexes become sluggish and, by the time the fever has attained its height, or shortly thereafter, they cannot be elicited. They return as the temperature falls and convalescence is entered on, but again tend to disappear if a relapse occurs. In children this finding is far more variable.

The Odour: There is a characteristic odour about the typhoid fever patient, familiarity with and recognition of which is of great assistance to the clinician. Experienced nurses will often arrive at a correct conclusion from this fact alone. The odour cannot be adequately described, yet it is distinctive and should be sought for.

Nervous System Manifestations: Headache is a constant symptom. It is usually frontal, dull in character and varying in severity, commencing early and often persisting after the disease is well established.

Delirium, when present, is of a quiet type, the patient requiring very little restraint. Stupor varies with the degree of toxæmia.

Delirium and the "typhoid state" are not very common in the Brisbane cases, and it must be borne in mind that these symptoms are not peculiar to typhoid fever. They tend to occur, however, in patients suffering from severe toxæmia and under-nutrition; if fluids and nutriment are taken freely, the incidence of these manifestations is greatly reduced.

Laboratory Examination.

The Widal Reaction: The Widal test is of doubtful diagnostic assistance. Often it does not yield a positive result until late in the disease or in the stage of convalescence, while the presence in the community of a large number of persons who have been inoculated and whose serum in consequence still reacts to the Widal test, may prove misleading.

Leucopenia: Leucopenia or, more frequently, absence of leucocytosis, accompanied by increase in the percentage of lymphocytes, is the rule. This, of course, may be altered by the incidence of any of the usual complications.

Blood Culture: Culture of the bacillus from the blood is of the greatest value. In the hands of a capable bacteriologist a culture is positive in a great majority of cases. This investigation should be carried out within a week of the onset, as it is during this period that the bacillus is most frequently isolated and as this is usually the stage at which the greatest difficulty is experienced in establishing a correct diagnosis, the procedure should not be omitted.

Stools and Urine: Culture of organisms from the stools and urine has led to isolation of the *Bacillus typhosus* on occasions so rare that from a diagnostic point of view it is of little assistance.

Differential Diagnosis.

Many conditions are mentioned under the heading "Differential Diagnosis." The diseases most likely to lead to confusion are those discussed hereunder.

Influenza: Influenza may simulate mild typhoid fever with bronchial symptoms. Leucopenia also is often present. The greater remissions of temperature, the presence of active abdominal reflexes, the condition of the tongue and stools, combined with observation for a day or two, should prevent error.

Miliary Tuberculosis: Miliary tuberculosis may present a picture closely resembling that of typhoid fever, but the general appearance of the patient, the tendency to cyanosis, the greater remissions of temperature, the increased pulse rate, the presence of the abdominal reflexes and absence of the characteristic odour should suffice to differentiate it.

Typhus Fever: The sudden onset of typhus fever, the abrupt rise of temperature, the rapid pulse, early toxæmia, the character of the rash, combined with leucocytosis and a positive Weil-Felix reaction, distinguish this disease.

Septicæmia and Endocarditis: Septicæmia and endocarditis may cause difficulty, but the irregular fever, rapid pulse, polymorphonuclear leucocytosis and blood culture serve to differentiate.

Appendicitis: A very occasional case of typhoid fever may be difficult to distinguish from appendicitis; rigidity of the abdominal muscles, however, is rare and a leucocyte count revealing leucopenia instead of polymorphonuclear leucocytosis would be suggestive of typhoid.

Paratyphoid Fever: Paratyphoid fever can only be distinguished serologically.

Conclusion.

In conclusion it must be stated that while many of the above statements are at variance with text book teaching, nevertheless they are founded on observations of the disease as it exists in this community.

ALEX MURPHY, M.C., M.B., Ch.M.,
Honorary Physician, Brisbane Hospital.

British Medical Association News.**SCIENTIFIC.**

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Medical Society Hall, East Melbourne, on October 29, 1930.

Cinematograph Demonstrations.

Cinematograph films were shown illustrating movements of the alimentary tract in laboratory animals, the influence of drugs on gastro-intestinal motility, the action of cholecystokinin, the treatment of Colles's fracture.

The Relation of the White Blood Cells to the Development of Malignancy.

DR. T. CHERRY read a paper entitled: "The Relation of the White Blood Corpuscles to the Development of Malignancy" (see page 275). The paper was illustrated by lantern slides and dealt with further results of Dr. Cherry's work on cancer in mice.

In discussing Dr. Cherry's paper, PROFESSOR AGAR asked if Dr. Cherry had ever prepared a chart of tuberculosis mortality according to race, as distinct from occupation.

MR. B. T. ZWAR paid a tribute to the value of Dr. Cherry's work and said that when Mr. Sampson Handley, of the Middlesex Hospital, was in Melbourne in 1929 he visited Dr. Cherry's laboratory, and remarked that he considered it most important that work of this type should be continued. Work carried out by an independent worker might even be productive of better results than when a number of workers were working together as in various research institutions.

Dr. Cherry in reply to Professor Agar said that he had never prepared a chart of tuberculosis mortality according to race as compared with occupation. He added that statistical information as to occupation was not so full in other countries as in England and that generalization could not be made from a study of the statistics in Australia as the numbers were not sufficiently large.

Dr. Cherry remarked that no tumours occurred in his mice during the outbreak of pseudo-tuberculosis; he believed this to be due to the condition of polymorphonuclear leucæmia. He had felt handicapped in his work by his isolation from other research workers in mouse cancer.

A MEETING OF THE QUEENSLAND BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Brisbane Hospital, Brisbane, on September 5, 1930. The meeting took the form of a series of clinical demonstrations by the members of the honorary staff.

Thrombo-Angilitis Obliterans.

DR. C. A. THELANDER showed a male patient aged thirty-seven years, a house painter, who had consulted him on November 24, 1926, complaining of sore lumps in both legs below the knees. At that time one lump was present in the right calf and three lumps in the left peroneal region. The lumps were the size of an almond kernel or a little bigger, were red, brawny and tender, and were situated on the veins. The patient's previous health had been good. He denied any venereal infection. He ate and slept well. He had not worked for the previous two days on account of the pain. Prior to that he had been at work. He thought his present condition dated from June, 1926, when he was bitten by a dog in the right leg; the

bite became inflamed. Since then he had had sore lumps in various places in the lower limbs. The provisional diagnosis was thrombo-phlebitis. He was referred to Dr. Duhig for a blood culture; no organisms were grown. His condition improved with rest and local painting with ichthyol, and he was able to work after a period of about two weeks.

On March 7, 1927, he again reported, stating that he was fairly well. On April 28, 1930, he reported that he was still getting "phlebitis," by which he meant sore lumps as above described. He also complained that his legs became cramped if he walked more than a mile. The right great toe sometimes felt lifeless. He felt cramps under the right foot.

He was spare, but had a healthy colour and was alert. Varicose veins were present on both legs, but were more pronounced on the right leg. There was a small inflamed patch on the outer aspect of the right instep, resembling exactly the former lumps which were thought to be due to thrombo-phlebitis. There was well marked fibrillary twitching of the *flexor brevis* muscle of the right foot. The toes were of normal appearance, but were rather cold.

The patient was referred to Dr. N. Markwell, who, on May 12, 1930, reported a diagnosis of *endarteritis obliterans*. He stated that there was no pulsation of the arteries below the right knee. The blood did not react to the Wassermann test.

On May 13, 1930, under local anaesthesia induced by means of "Novocain" infiltration, alcohol was injected into the *tunica adventitia* of a section of the femoral artery, about five centimetres (two inches) long in Scarpa's triangle. The artery was rather small when exposed, its external diameter being about seven millimetres. By the conclusion of the operation it had contracted to about five millimetres.

On May 14 the patient complained of a lot of pain. On May 19 the wound was healed well enough for him to be allowed to leave hospital. On May 27, 1930, the patient reported that he was no better. He was advised to have a sympathectomy performed. He had given up tobacco and was taking potassium iodide and nitroglycerin. On July 26, 1930, he reported that there was no improvement at all and that an ulcer had developed on his instep. The cramps in his leg were worse than ever, the toes were bluish and blanched and the foot felt cold. On August 4, 1930, under general anaesthesia given by Dr. Markwell, Dr. Thelander, assisted by Dr. Meyers, performed a right lumbar sympathectomy through the right lumbar approach. Three ganglia were removed and the trunk and four rami were divided. The day following operation the patient stated that he felt a few cramps, but the foot felt warmer. There were no cramps from that time onwards, and on August 13 some pulsation was felt below the knee. At the time of the meeting the condition was not satisfactory. The case was of unusual interest because the condition was associated quite definitely in the patient's mind with the dog bite. The ulcer on the leg had healed.

Injuries to the Elbow Joint.

DR. H. CRAWFORD, with the permission of Dr. G. A. C. Douglas, showed six patients who had had severe injuries to the elbow joint.

As the result of a blow, the first patient had suffered a complete compound disorganization of the elbow. The ulnar nerve had been severed. The arm was cleaned at operation on July 1, 1930, and the bones replaced. At the time the arm looked as if an amputation would have to be performed. The patient now had very fair movement at the elbow joint, but there was a possibility of a false joint. The arm, however, was a useful one.

Dr. Crawford's second patient was a male, aged nineteen years, who had been admitted to hospital on June 5, 1930, with a history of a blow on the elbow five days previously. At the time of admission there was a "T" shaped fracture and considerable deformity. Operation was performed on June 9, 1930, when the elbow was readjusted and the two lower fragments fixed together with kangaroo tendon.

The third patient was a male, aged thirteen years, who had been admitted to the hospital on May 19, 1930. He

had fallen on his elbow. A plaster was applied at the time and an open operation was performed on May 27, 1930. There was a fracture of the olecranon at the epiphyseal line. This was reduced and the wound cleaned and sutured.

The fourth patient had been admitted on January 8, 1930, with a compound fracture of the lower end of the humerus. On January 14, 1930, manipulation was performed and a plaster splint applied. On January 24, 1930, an open reduction was performed. The fragments were drilled and united with kangaroo tendon. The arm was then fixed in flexion with a plaster splint.

The fifth patient was a male, twenty-five years of age, who had been struck on the right elbow by a tram, a compound fracture resulting. The wound was cleaned and fragments of bone were removed. The remaining fragments were readjusted in position. A plaster splint was applied.

The last patient was a male, aged nineteen years, with a "T" shaped compound fracture of the lower end of the humerus into the joint; there were rotation forwards and anterior displacement of the fragments. Two operations had been performed. The first was on June 21, 1930, the second on June 30, 1930. At the second operation the fragments were replaced in position and fixed with kangaroo tendon. The limb was then fixed in a plaster splint.

Dr. Crawford remarked that he showed this series of severe injuries to the elbow joint to demonstrate that treatment of such injuries was satisfactory. One could look forward to a fair result, judged by the return of movements and function, even when the injury was most severe.

In the treatment of compound fractures in the elbow region, it was necessary in the first place to sterilize the skin and wound and remove all devitalized tissues. If the fracture involved the joint, the joint surfaces of the bones should be properly adjusted; this could be done at the second operation. The fragments should be brought together and fixed, if necessary by kangaroo tendon sutures; as a rule it was found that suture of muscle and periosteum sufficed to hold the fragments in apposition. The limb should be fixed for a time in the position best suited for maintaining accurate apposition of the fragments; the hand should be fixed in moderate pronation in view of the possibility of loss of movement at the elbow joint. If the patient were seen within a reasonable period following the accident, primary suture should be done. Dr. Crawford advocated the institution of early movement of the joint; the risk of non-union was much less than the risk of loss of movement. When the fracture was not compound and the fragments could not be adjusted, there should be no hesitation in treating by open reduction, either immediately or after ten days.

Pernicious Anæmia.

DR. N. W. MARKWELL showed a male patient suffering from pernicious anæmia. At the time of his admission to hospital in January, 1930, his red blood cells numbered 1,920,000 per cubic millimetre and examination of his blood revealed a typical picture of pernicious anæmia. The administration of liver led to great improvement; in March, 1930, the red blood cells numbered 4,690,000 per cubic millimetre. On August 29, 1930, he complained of itching over the front of his chest; his skin was very red. It was found that he was very enthusiastic and was in the habit of taking 336 grammes (three-quarters of a pound) of liver per day. His symptoms were ascribed to this. The amount of liver was reduced to 112 grammes (a quarter of a pound) daily. His colour was now much better. His red blood cells now numbered 5,180,000 per cubic millimetre and he still complained of itchiness of the skin of his chest. Dr. Markwell said that apparently there was wisdom in the recommendation to raise the red cell count to four and a half million per cubic millimetre.

Malarial Treatment.

DR. JOHN BOSTOCK showed two patients in whom malarial treatment had been used. Both patients were suffering from general paralysis of the insane. The first patient was a male, aged twenty-two years. His voice had become dull, his tongue was tremulous, with a coarse to-and-fro

movement. The pupils were unequal and did not react to light; the knee jerks were absent. Both the blood and the cerebro-spinal fluid reacted to the Wassermann test.

The second patient was a girl who had been very sick. The Wassermann reaction on the blood was strongly positive. In addition to the malarial treatment, the girl was having injections of "Tryparsamide" with considerable benefit. She was now able to help a little in the ward.

Lymphadenoma.

DR. A. P. MURPHY showed a man, aged thirty-four years, who had been admitted to hospital on July 27, 1930, complaining of a swelling in the neck and pain in the pit of the stomach for three weeks. There was nothing of importance in the past history. The patient stated that his health had been good until one year previously, when he had had a similar illness, with pain and swelling of the right side of the neck and pain in the abdomen. Three months before admission he had suffered from pain in the epigastrium and swelling and pain in the left side of the neck. This had been associated with headache, loss of appetite and general malaise. One week prior to admission he had felt much worse and was unable to take food for one week. He had had no difficulty in swallowing; the pain in the epigastrium was not associated with taking food.

He was poorly nourished and had an anxious expression. The cervical glands were discretely enlarged and not tender. There were several enlarged axillary glands. The liver was enlarged and the spleen was slightly enlarged. On July 29, 1930, radiological examination of the chest revealed dulness at the base of the right lung and an area in the right lung suggestive of fluid. There was a shadow in the upper part of the heart region and it was difficult to differentiate which was the heart shadow and which was extra shadow. The red blood cells numbered 3,200,000 per cubic millimetre, the white cells 10,200 per cubic millimetre. The hæmoglobin percentage was 65 and the colour index was 1.0. The percentage of polymorphonuclear cells was 83, lymphocytes 11, large mononuclear cells 2, eosinophile cells 4. Polychromasia was present. There was no reaction to the Wassermann test.

On August 2, 1930, X ray examination revealed that the shadow on the right side had increased to a much greater extent upwards, so that the mediastinal space had been obliterated in the lower two-thirds. The body temperature was continuously above normal.

On August 7, 1930, a cervical gland was removed. Histologically it had the appearances of advanced lymphadenoma. The characteristic features were a reticulo-endothelial proliferation to the stage of fibrosis, some scanty red cells and an abundant eosinophile exudate.

On August 16, 1930, the right pleural cavity was aspirated. Examination of the fluid revealed no tubercle bacilli or pus cells. Attempts at culture were fruitless.

On September 4, 1930, the red blood cells numbered 1,830,000 per cubic millimetre, the white cells 2,500 per cubic millimetre. The hæmoglobin percentage was 36 and the colour index 1.0. Anisocytosis, diffuse polychromasia and slight punctate basophilia were present. The blood platelets numbered 320,000 per cubic millimetre.

Deep X ray therapy was being given to the mediastinal, paraaortic and epigastric glands.

DR. EUSTACE RUSSELL showed an unmarried male patient, aged forty years, who had been admitted complaining of painless swellings on both sides of the neck, more advanced on the left side. He had had a cough some years previously. At the time of admission he had no sore throat, no scratches on face or neck, no visible ulcer, no cough and no glands anywhere else in the body. He was very well and was gaining weight. He was a large, healthy looking man. After excluding other possibilities, a diagnosis of Hodgkin's disease was made. Hodgkin's disease, syphilitic glands, tuberculous glands, malignant glands, lymphosarcoma and aleucæmic leucæmia should be considered. The Wassermann reaction was strongly positive.

Histological examination of a gland revealed a granulomatous type of growth associated with fibrosis and giant cell formation, similar to that of gummata. In

spite of this, Dr. Russell still considered Hodgkin's disease was the correct diagnosis.

The red blood cells numbered 5,000,000 per cubic millimetre. There was no abnormality in the cells of the blood. In Hodgkin's disease there were generally a definite anaemia, a leucocytosis and eosinophilia. Dr. Russell said that this patient was undoubtedly syphilitic and probably had lymphadenoma at the same time.

Erythema Multiforme.

Dr. Russell's second patient was a boy admitted six weeks before the meeting in a very serious condition. When first seen, he was cyanosed and had huge blotches on the face, arms and legs. He had meningismus. A diagnosis of cerebro-spinal meningitis was made. A lumbar puncture was performed and a fair amount of cerebro-spinal fluid was obtained. Examination of the fluid revealed no abnormality.

After this the boy commenced to improve and the condition resolved itself into *erythema multiforme*.

Pylorectomy.

Dr. E. S. MEYERS showed a man on whom gastro-enterostomy had been performed in Townsville ten years previously. A pylorectomy was performed by Dr. Meyers. Three weeks after the operation the patient was affected with a fever. Different suggestions were made, but the patient settled down without much trouble. Later, his chest was examined by means of X rays and extensive tuberculous disease was found.

Tumour of Rectum.

Dr. Meyers also showed a male patient who had been admitted on May 16, 1930. He had suffered from increasing constipation during the previous five months and a slight amount of discharge from the anus. He had had a Neisserian infection.

He was found to have an extensive fungating tumour in the anus and there appeared to be an inoperable tumour of the rectum.

At laparotomy an extensive growth from the pelvi-rectal flexure of the bowel downwards was observed. Thirty-seven milligrammes of radium were inserted. Radium was also inserted along the rectum.

The Wassermann reaction was strongly positive, but antisyphilitic treatment had been unsuccessful. At the time of the meeting the anus appeared normal and the patient had gained 9.45 kilograms (one and a half stone) in weight. Two sections were obtained and examined. One had the appearances of a gumma, the second a non-malignant papilloma. Clinically the growth had appeared malignant.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association:

Burston, Geoffrie Carthew, M.B., B.S., 1929 (Univ. Melbourne), Cliff Road, Frankston.

White, Salome Jean, M.B., B.S., 1929 (Univ. Melbourne), Children's Hospital, North Adelaide, South Australia.

Dungan, Rae William, M.B., B.S., 1930 (Univ. Melbourne), Gippsland Hospital, Sale.

Baker, Aubrey Wilfred, M.B., B.S., 1930 (Univ. Melbourne), Geelong Hospital, Geelong.

Hurley, Edmund Reginald, M.B., B.S., 1929 (Univ. Melbourne), Geelong Hospital, Geelong.

Correspondence.

THE HOSPITAL PROBLEM.

SIR: In his timely letter on this subject in your issue of February 7, Dr. E. S. Meyers urges the necessity for some cooperative effort by the members of our association to grapple with the many and involved problems confronting our hospitals.

So far, the Australian Branches of the British Medical Association have made very little attempt, either separately or collectively, to survey and define the particular hospital problems of their respective States and they have yet to follow the lead given by the parent body when last year it set out its new hospital policy very clearly in the columns of *The British Medical Journal*. That policy contains many pertinent facts and modern ideals which, with a little modification, could be applied to the various hospital systems in Australia.

The hospitals are the workshops of the medical men and surely the latter should give a lead to the rest of the community in putting them on a permanently secure and orderly running basis. Little can be expected from politicians and lay hospital committees without expert guidance, because they do not possess even an elementary knowledge of hospital management. Many do not realize that running an efficient hospital is just as intricate a business as running a successful hotel or guest house, with the added provision of bedside, sanitary and nursing service for each guest. Even Henry Ford could not show a profit on his well known hospital in Detroit when faced with the great overhead expense of X rays, pathological and other diagnostic services; and his scale of fees (in advance) would make the average Australian hotel manager turn green with envy.

It is often alleged that doctors are bad business men, but, through their association, they should at least be able to tell State governments what constitutes an ideal hospital system and then follow up their statements by energetic propaganda and community influence until success is achieved.

I realize that finance is a big stumbling block, but there are signs that the community is waking up to the fact that the adequate care of its afflicted is one of its cardinal obligations, just as much as is the education of its children and the administration of its laws. These two latter services are a direct charge on the taxpayers—then why not good community hospitals where the poor can be treated in wards at low rates and the rich and near-rich in accommodation suitably graded to the depths of their pockets?

Hey Groves remarked in a recent article on British hospital systems that soon the honorary system for medical staffs would be as dead as the dodo. It is half dead now and its final demise will come when we have a reorganized plan of hospital operation born out of the present chaotic and haphazard muddle.

Let us put aside the old platitude that "something must be done" and let our respective Branch hospital committees get down to action by: (a) Defining briefly and clearly the outstanding points of the hospital problem in each State. (b) Publishing a definite hospital policy for our association, modified, if necessary, for each State and backed by a forceful organizing campaign among all our members. (c) Forming a hospital section for the next association congress and inviting the cooperation of hospital superintendents and chief executives.

These are a few constructive suggestions and indicate preliminary steps which might be taken to interest the members of our profession in a problem which affects them vitally. Then, I am sure, there would be no further grounds for complaint that hospital policies failed to evoke general discussion.

THOMAS HAMILTON.

Newcastle,
February 13, 1931.

WORKERS' COMPENSATION.

SIR: The admirable summary of the clauses of the *Workers' Compensation Act* (N.S.W.) in last week's journal (page 211) contains the following in reference to railway employees:

The Railway Commissioners are self-insurers and will pay the medical attendant of an injured employee entitled to compensation and cost of treatment direct, subject to his charges being in accordance with Schedule D.

For the enlightenment of any other medical practitioner who may be called upon to treat injured railway workers, the facts in the following case may be interesting and disillusioning.

A railway worker, B.H. McK., was seen by me on January 12 last, with a direct inguinal hernia which, he stated, had that day suddenly appeared at work. I sent him to the Railway Medical Officer who concurred in the diagnosis and the causal relationship of his work and advised operation. I verified these facts by telephone conversation with the Railway Medical Officer and, on his advice, duly did a radical operation in a private hospital.

I forwarded an account to the Railway Department in accordance with Schedule D, namely, operation twelve guineas, anæsthetic three guineas, and duly received the following sweeping reply:

I have to inform you that it is not considered the Department is liable for medical costs incurred for treatment rendered at any hospital, and that being so it is regretted the case is not one in which payment of the amount claimed can be authorized.

Yours, etc.,

R. D. DAVEY, M.B., Ch.M.

5, George's River Road,
Croydon Park,
February 18, 1931.

TONSILLECTOMY.

SIR: I was amazed to read in the leading article on "Tonsillectomy" in THE MEDICAL JOURNAL OF AUSTRALIA of February 7 certain statements which are both incorrect and damaging to those surgeons whose method of performing the Sluder operation results in complete enucleation of the tonsil.

The article in question states: "Sluder's operation, though easy of completion, always results in incomplete removal of the tonsil. The lower pole remains." Further, in reference to Sluder's operation, the article states: "It should be used with the full knowledge that it results in incomplete removal of the tonsil and that a second operation may be necessary."

Could any more damaging statement be made?

As an advocate of the Sluder operation, I felt I could not let these statements pass unchallenged. In my opinion the Sluder operation is the operation of choice in roughly 80% of cases, the balance being better treated by either dissection or diathermy. The operation of choice in this latter group depends on the nature of the tonsil and the wishes of the patient.

Now, as regards the type of case suitable for complete enucleation with a blunt guillotine by Sluder's operation. A detailed examination of the tonsil will reveal:

1. Whether the lower pole is a definite entity or whether it consist of a long attenuated process, extending variable distances down the pharynx. It will be found in the majority of cases that the lower pole is a definite entity and that with proper manipulation it can be completely engaged in the guillotine together with the upper pole.

2. Whether the tonsil is "enucleable," that is, whether it is more or less "mobile" in its capsule. This can be readily ascertained by either of two methods: (a) By turning back the anterior pillar and gently pushing the blunt end of a small flat instrument behind the tonsil. In the majority of cases the instrument meets with little resistance and the tonsil readily bulges into the throat. (b) By pressing the tip of the index finger on to the anterior pillar just external to the tonsil that sense of mobility can be detected.

Quinzy, of course, is the commonest agent which anchors the tonsils and makes the operation more difficult.

Although this contribution is more in the nature of a letter of protest, a word as to the technique employed may not be out of place.

Anæsthesia is a little deeper than that usually employed for the Sluder operation. A Doyen's mouth gag is used. The patient's head is held well back by the anæsthetist, who also steadies the gag and turns the head slightly towards the patient's right, the right tonsil being the

first to be removed. The operator stands on the patient's right. The assistant (usually the theatre sister) is on the patient's left. She manipulates the sucker, a spatula and several sponge-holders with woollen swabs wrapped in gauze, picked out as nearly as possible the same size as the tonsils to be removed. The requisite sized guillotine is chosen, the lower pole of the tonsil is engaged first and then the upper pole is massaged through the guillotine with the thumb of the left hand. The thumb is used, the ball of this digit being larger than that of any of the fingers, is consequently better able to control the tonsil after it is completely engaged in the guillotine. The upper pole can be felt to pass through the guillotine with a characteristic "plomp." The same thumb still holding the now completely engaged tonsil is gently rotated so that the line of reflection of the anterior pillar on to the tonsil can be seen. The blade of the guillotine is now closed on to this line. The complete tonsil is now engaged in the closed guillotine, the closing of the blade approximating the anterior and posterior pillars behind the tonsil and capsule. The thumb is now removed and the pillars are separated from the tonsil by the index finger of the left hand. The instant that the tonsil is removed the assistant plunges one of the swabs held in the sponge-holder into the tonsil fossa, at the same time using the sucker to remove any blood which may obscure the field for the removal of the second tonsil. The operator now changes his position to the right head of the table.

The swab still being held in position, the patient's head is now turned slightly to the left. It may be necessary at this stage for the assistant to depress the tongue. The left tonsil is now engaged in the same manner as the right, the only difference being that in the case of the left tonsil the pillars are separated with the thumb of the left hand. The operation takes about one minute and a half.

All adults are given calcium lactate, thirty grains three times a day after meals for three days prior to operation and one dose on the morning of the operation.

To sum up, it is claimed that 80% of cases are suitable for the Sluder operation, that their tonsils are completely removed, that the lower pole does not remain. The remaining 20% are not suitable for the Sluder operation, but should be treated either by dissection or diathermy.

For the sake of my own reputation and that of my many colleagues who adequately perform the Sluder operation, I am taking the liberty of sending you a bottle containing some thirty odd tonsils removed by the method as described above. Will you be good enough to submit these tonsils for examination to any leading nose and throat specialist and if, in the opinion of the specialist of your choice, they have been adequately removed (complete with capsule and lower pole) I think it is only reasonable to ask that the passages objected to in your leader of February 7 should be refuted.¹

Yours, etc.,

FRANK W. FAY,

M.C., F.C.S.A., M.B. et Ch.B.

174, Macquarie Street,
Hobart,
(Undated).

POST-GRADUATE WORK.

SIR: I think it desirable to bring under the notice of the medical profession of Australia the action taken by the Sun Life Assurance Company of Canada. This insurance company has provided, for six years, £6,000 a year. The money is used to send speakers all over Canada to address medical associations and is really a form of post-graduate education. It is interesting to note that in Australia our post-graduate work is effected by bringing the medical practitioners to the cities. In Canada the reverse process has been adopted, owing to the generosity of the Sun Life Assurance Company, who realize the importance of the work from their point of view. The following table shows what has been done.

¹ The tonsils referred to by Dr. Fay may be seen at the office of the journal.

Year.	Number of Speakers.	Number of Addresses.	Average Attendance.	Total Attendance.	Total Cost.	Cost per Lecture per Doctor.
1926	160	513	29	17,264	\$6,020 approx.	7s. 0d. approx.
1927	269	729	27	19,683	\$5,766 "	6s. 0d. "
1928	329	802	31.7	25,423	\$6,667 "	5s. 0d. "
1929	379	730	36	26,287	\$6,251 "	4s. 9d. "
1930	300	580	38	22,036	\$5,592 "	5s. 0d. "

I am indebted to Dr. Routley, Secretary of the Canadian Medical Association, for this information.

Yours, etc.,

JAMES W. BARRETT.

103-105, Collins Street,
Melbourne,
February 2, 1931.

THE UNION OF EPIPHYSES.

SIR: Regarding the letter from Dr. Palmer in your issue of January 3. In making notes of the age of appearance and fusion of epiphyses, all the centres enumerated by Dr. Palmer have been found fused in girls aged fourteen or younger, except in the cases of the second, third, fourth and fifth metacarpal bones, which have not been seen in girls under fifteen years of age. Moreover, fusion has been found to occur in the majority of Australian girls aged fourteen or under in all the epiphyses enumerated except those of the acromion process and upper end of the tibia, which fuse usually at fifteen, all the metacarpals, which fuse at sixteen, and the head of the femur, which fuses at seventeen.

As stated by Dr. Palmer, these dates are much earlier than those usually quoted, but they do not differ greatly from those described by Galstaun in the case of Hindu girls.

Yours, etc.,

H. FLECKER.

71, Collins Street,
Melbourne,
February 16, 1931.

TEETH EXTRACTION.

SIR: Is it not time a halt was called in regard to the ordering of wholesale extraction of teeth by medical men on insufficient grounds? I have repeatedly seen patients who have been urged to have all their teeth extracted, the only abnormality being a slight gingivitis. Surely such advice in the absence of marked looseness of the teeth or of X ray evidence of apical trouble, is clearly empirical. I am quite satisfied that in many cases the opinion that the patient's teeth need extracting is a refuge and not a diagnosis. The *sang froid* with which some medical men urge wholesale extraction almost makes one think that they believe the patient will promptly erupt another set!

There are serious mechanical and other disadvantages attached to the wearing of artificial teeth, and I suggest that this fact is frequently overlooked.

Yours, etc.,

R. N. BURTON.

Texas,
Queensland,
February 2, 1931.

SPRUE ASSOCIATED WITH AMEBIC DYSENTERY.

SIR: Dr. Gutteridge and I much appreciate the interest shown by Dr. W. L. Calov in the recent case of "Sprue Associated with Amebic Dysentery" reported by us.

In a communication such as ours it is impossible to give full details. The patient was undoubtedly suffering from

sprue. To quote from Manson: "The condition of the tongue, character of the stools and history are sufficiently distinctive . . . to render diagnosis an easy matter."

On reference to my notes I find that there was some distension of the abdomen, but no tenderness in that region; liver dullness was somewhat diminished.

The bowels were frequently opened and the stools, large, pultaceous masses, not liquid and not formed; they were fatty and grey in appearance (probably we erred in describing them as "tan," but followed Dr. Edwards Jenner Wood's term in his article on sprue in the recent edition of "Osler's Modern Medicine").

We did not carry out chemical examinations of the stools and blood; this case was investigated and treated in private practice. In reply to the questions of Dr. Calov:

1. The appearance of the skin was that of a severe grade of anemia with loss of all subcutaneous fat and numerous petechial hæmorrhages.

2. I have described the abdomen, in which the only outstanding features were the distension, most marked in the lower region, and the decrease in liver dullness.

2. The chemical composition of the stools was not investigated.

4. The diet was varied; at first he was kept altogether on milk, which was pushed; gradually such articles as porridge, groats and other such foods were added. Liver, minced and in soup, and mashed bananas were introduced. After the first blood transfusion the appetite was greatly increased—described as "ravenous." Two weeks later he lost the desire for food, but this was renewed following the second blood transfusion, when, during convalescence, bacon, white meat, brains, tripe, mashed potatoes, pumpkin, marrow, mutton and milk puddings were also given. One and a half dozen bananas each day was a standing order.

We claim nothing original in our investigation and treatment of this case and would apologize for lack of some data, but consider that it was of interest, as it demonstrated: (i) The development of a condition in all respects of sprue following on an acute attack of dysentery and associated with the presence in the fæces of the cysts of the *Entamæba histolytica*; (ii) the beneficial effect of emetine bismuth iodide followed by repeated blood transfusions. In conditions such as this, which closely resembles pernicious anemia in many respects, we also consider that liver should be given a place in the dietetic treatment.

Yours, etc.,

HAROLD CRAWFORD.

Wickham Terrace,
Brisbane,
February 14, 1931.

Post-Graduate Work.

PRIMARY FELLOWSHIP EXAMINATION OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND.

A NOTICE has been received from the Secretary of the Royal College of Surgeons of England to the effect that the primary examination in anatomy and physiology for the Fellowship of the Royal College of Surgeons will be held at the University of Melbourne on Tuesday, August 11, 1931, and following days.

Copies of the regulations, schedules of the required certificates and further particulars may be obtained from the Honorary Secretary of the College of Surgeons of

Australasia, 6, Collins Street, Melbourne, or from the Director of Examinations, The Examination Hall, Queen Square, London, W.C.1, England.

COURSE OF INSTRUCTION IN ANATOMY AND PHYSIOLOGY.

A COURSE of instruction in anatomy and physiology will be given at the University of Sydney, commencing on April 7 and terminating early in August. The course has been arranged especially for candidates for the primary fellowship examination of the Royal College of Surgeons of England, but other graduates may attend.

The lecturers will be:

Anatomy: Dr. H. Poate, Dr. F. A. Maguire, Dr. V. M. Coppleson, Dr. D. Miller, Dr. P. Braddon.

Physiology: Dr. A. J. Canny.

There will be at least two tutorial classes a week in each subject. The time table will be arranged by the lecturers after consultation with the class. The fee for the complete course will be twenty guineas. Candidates who require dissecting parts must in addition pay the usual university fees for these to the Registrar of the University.

Prospective candidates must notify the Registrar, the University, on or before March 14 of their intention to attend this course of instruction and must enclose a cheque for the fee. Candidates are reminded that it is necessary to enter for the examination on or before March 31, 1931. Entrance forms are obtainable from the Secretary of the College of Surgeons of Australasia, 6, Collins Street, Melbourne.

Obituary.

MORRIS FREDERICK HORSLEY GAMBLE.

We regret to announce the death of Dr. Morris Frederick Horsley Gamble, which occurred on February 23, 1931, at Kew, Victoria.

Medical Appointments.

Dr. P. S. Messent (B.M.A.) and Dr. A. R. Southwood (B.M.A.) have been appointed members of the Dental Board of South Australia.

Dr. J. G. Sleeman (B.M.A.) has been appointed Medical Superintendent of the Adelaide Hospital, Inspector-General of Hospital Department, Division 2, under the provisions of the *Public Service Acts*, 1916 and 1925.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, locum tenentes, sought, etc., see "Advertiser," page xiv.

PERTH HOSPITAL, PERTH, WESTERN AUSTRALIA: Junior Resident Medical Officers.

REPATRIATION COMMISSION: Resident Medical Officer.

ST. MARGARET'S HOSPITAL FOR WOMEN, SYDNEY, NEW SOUTH WALES: Pathologist.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company, Limited. Phoenix Mutual Provident Society.
	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	Members desiring to accept appointment in ANY COUNTRY HOSPITAL, are advised to submit a copy of their agreement to the Council before signing, in their own interests. Brisbane Associated Friendly Societies' Medical Institute. Mount Isa Hospital. Mount Isa Mines.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Contract Practice Appointments in Western Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	Friendly Society Lodges, Wellington, New Zealand.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

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